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THE HOSPITAL'S RESPONSIBILITY IN PREVENTIVE MEDICINE

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Ruhräh reminds us that the three patron saints of prophylactic pediatrics are Pemell, Cadogan and Armstrong. Armstrong, in 1769, when he created his Dispensary for the Infant Poor, said, "I did not confine myself to the therapeutic or curative part of physic only. I likewise extended my care to the prophylactic branch, or that which concerns the prevention of disease." Caulfield's comment on Armstrong's Dispensary is that "no charitable institution was ever established whereby so much good has been done, or so many lives saved at so small an expense."

In the past, the appeal to a hospital was to heal; at the present, the command to the hospital is to prevent. The day is here when all hospitals treating children should be actively interested in prophylactic pediatrics as well as in the restoration of the sick child to health, for the prevention of disease is both an important and a practical function of a children's hospital, and it should not evade its obligation in the premise. The pediatrician, having received an elaborate specialized education and having been given the opportunity to direct the beginning of the child's life, has the responsibility to further the prevention of disease. Naturally, this should be done at the source from which he acquired his training and experience, a children's hospital.

A children's hospital's sphere of activity should cover all aspects of pediatrics, giving first consideration to the child himself. If the child coming to the hospital is to have adequate care, the professional staff must have an ecologic point of view of the child and his environment, one embracing his physical, mental and emotional background. Altogether too common in a children's hospital is the failure to take into account the entire child and his environment. We have a tendency to limit our consideration to some circumscribed pathologic problem, and we will do well to broaden our vision. A hospital is fortunate indeed if

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the members of its staff think of the child psychobiologically and sociologically: if its physicians and nurses think of the whole child and appreciate that his whole body is involved in everything he does and that the child responds as a whole. A comprehensive consideration of the child on the part of a children's hospital can best be effected by the creation of a department devoted to the prevention of disease.

A department for the prevention of disease in a hospital should prove a fertile field in which to conduct research on growth and development because of the possibility of continuing observation and obtaining complete records throughout the period of childhood. A distinct division for preventive medicine would afford the opportunity of investigating the active underlying factors causing poor health, because medicosocial investigation of the child's environment may disclose the combination of circumstances responsible. It is necessary not to devote less time in studying the end-results of disease processes, but to devote more attention to those subjects which are of etiologic significance. The hospital staff should initiate research in child hygiene, as the hospital is the only agency fully equipped to carry out such an investigation, and in the hospital's organization a department for child health is the logical place where it could be instituted. As yet, however, little research in the field of child hygiene has come from hospitals.

Preventive medical services for supposedly well infants and children might well be conducted in prophylactic clinics such as a health clinic, a parental guidance clinic, a nutrition clinic and a clinic for posture, oral hygiene and the prevention of rachitis, tuberculosis, diphtheria, smallpox, blindness and deafness.

All children discharged from the outpatient department as cured should be referred to a health clinic in the department for the prevention of disease. Here each child's study would be continued through periodic physical examinations and by supervision of his home conditions. The supposedly well child coming to the hospital should be separated from the sick child. Although there is a difference of opinion on this matter, it is obvious that disease contacts will thus be reduced. It is a practical fact that the approach by the medical staff must be entirely different in the two cases, and that the personality of but few clinic physicians permits them to adjust their psychologic processes quickly enough to meet the situation fully. The advice to be given the well child and his parents requires more time than the advice to be given the sick child's parents. In the former case, it must cover mental hygiene, home hygiene, personal hygiene and social responsibilities.

An important obligation for a prophylactic pediatric department would be the prevention of behavior problems, and this can be approached best through what is commonly understood by the term mental hygiene. Mental hygiene can be most satisfactorily carried on

in a parental guidance clinic established in this department where parents may be educated so that they may guide their child's personality development wisely. This clinic must meet beginning personality difficulties, such as protest reactions, harmful conditioned reflexes, negativism, a sense of inferiority, hypersensitivity, seclusiveness and fears, by searching out the actual motive for the asocial conduct.

It would seem as if too much emphasis at the present time is being placed on child guidance clinics and not nearly enough on the more important, and much safer, parental guidance clinics. Mental hygiene will succeed by correcting parental misconceptions and by helping parents to make whatever adjustments they themselves need as well as effecting such changes as may be necessary in the home, play and school life of the child. This indirect approach to the problem through the parents is usually successful, and certainly is more safe so far as it protects the child from advice that may be based on incorrect factual data.

Mental hygiene, unlike other types of medical care, has been chiefly enjoyed by those in favorable financial circumstances; nevertheless, many others less favored have received such help through nursery schools, family relief agencies, guidance clinics, private schools, social agencies, visiting teachers and research bureaus. While this country as a whole has a right to be proud of its research work in mental hygiene, it is to be noted with regret to what slight extent children's hospitals have interested themselves in this service. Quite the reverse has been the case among social agencies; for some years many have been actively interested. Materially, a children's hospital is better equipped than any other institution for mental hygiene work, although it generally lacks in personnel that most essential individual, the pediatropsychiatrist. The pediatropsychiatrist could guide parents to a realization of how they may best nurture their newly born infant egoists so they can in time acquire constructive moral and social attitudes. A hospital department for the prevention of disease would make an ideal laboratory in which to study the child's mental and emotional development. Can the hospital be aroused from its lethargic state before this opportunity for child study is appropriated by social and welfare agencies?

A hospital department for the prevention of diseases may have many functions. For example, it may act as the agent for the hospital in all matters between it and the public, whether pertaining to patients in the wards, children in the outpatient department or well children. It may offer health education to groups of parents and children of different ages, sexes and races, but it should be chiefly interested in teaching health to groups of children living in the neighborhood of the hospital and those who have been treated in the wards or the outpatient department.

In order to help the greatest number of parents and children, it is essential to have a health teacher. She should be a well trained public health nurse who is also thoroughly trained in modern methods of teaching children. The health teacher should organize and conduct classes and clubs of children of different ages. The essential objective of group health work should be to teach personal hygiene and to achieve the establishment of positive health habits for children. The parents of the children need to be taught child hygiene, the responsibility of the individual and the group in determining healthful types of amusement and recreation, good housekeeping, community health facilities and the prevention of infections. There is a great deal of truth in what Chesterton said, that "It is not so much people's ignorance that does the harm as the knowing of so much that ain't so!"

Health education is of such fundamental importance that children's hospitals would do well to give its establishment first consideration as a part of the work that offers large results in proportion to the effort expended. If ignorance is one of the chief causes of illness, then parental and child education in applied hygiene, broadly defined, is one of the hospital's most effective weapons. It will enable the hospital to carry the health message to thousands of children whom it would not otherwise be able to reach. Incidentally, the presence of a prophylactic department will have a remarkable psychologic effect on the community's feeling toward the hospital. Whether one believes it or not, the fact still remains true that it is the function of a children's hospital to keep well the children living in its vicinity, because it is the only agency with the indispensable equipment.

The department for the prevention of disease should conduct all the field work, both curative and preventive, whether it is educational, medical, nursing or social. The proper preparation of the home for the return of the child in the ward is a neglected hospital problem. One almost wonders what is the use of care in a hospital ward if the child is to return to the same unhygienic environment that was primarily responsible for its illness. The home of every outpatient child should be visited within twenty-four hours after his coming to the hospital, and his parents should be given the necessary instruction in the nursing care prescribed by the hospital physician. The home report made by the field worker should include the social situations that may have been responsible for the child's illness and the housing and economic condition of the family. A social diagnosis should be formulated which will give the physician a clear understanding of the patient's home surroundings, the intelligence of the parents and the environment to which the child must return after recovery.

One cannot agree with the criticism made of having registered nurses for follow-up work in the home. Is not a nursing education

really essential for field work from a children's hospital? The best field worker for a pediatric hospital is a graduate nurse who has had training in social work. No one dare say that a sociologic training could qualify one to teach personal and home hygiene, or to instruct a mother on the nursing technic to be used in the care of her sick child. Surely a hospital is not to incur the expense of sending two workers to the home, a nurse and then a social worker?

Preventive work ought to be confined to a small district surrounding the hospital for the practical reason that it would be far too costly for any one hospital to carry out health supervision over a large territory. The size of the staff required and the necessity of transporting field workers over a large territory would be prohibitive. Restricting the field of operation enables the hospital to get maximum results from the money designated for preventive work. Incidentally, the districts should be assigned so that they can be covered with the greatest saving of time and cost in transportation.

If every children's hospital would recognize its opportunity in preventive medicine, it would advance the standard of the welfare work of other agencies interested in the health of children. For the hospital has a real social obligation to the community as well as a medical one, and it must help to correct the social conditions that might have an injurious effect on child health. A department for the prevention of disease in a children's hospital will help to overcome some of the limitations of social service work, not by curtailing in any way the hospital social work, but by placing it under medical supervision. Social service departments not under direct medical supervision have been handicapped by a lack of knowledge of the true health status of the child even shortly after it has been discharged from the hospital. The only way this information may be accurately obtained is by extended medical supervision.

Hospital social service is still in a developmental state, and no uniform method applies to all hospitals. It is true that most children's hospitals worthy of the name do have social service departments, but one cannot help wondering a little how much the medical and nursing staff are really interested. An inadequately educated intern considers even reading the social diagnosis as something too useless to be allowed to intrude on his profound scientific cogitations. Without doubt, a rapidly increasing number of young pediatricians are finding the social survey illuminating, and are asking for more and more apposite data. Every problem concerning the child is so intimately bound up with both health and social problems that they cannot be separated. By correlating all the medicosocial activities of the hospital in a single department, the work would be done with greater efficiency. The

physician who does not feel the need of a sociologic understanding of his patients is outside the pale of modern pediatrics. This is equally true of a children's hospital, for a pediatric clinic without social work is almost valueless.

A monthly conference should be held in the department in order to bring together social agencies working for children. The subject of child care should be discussed in all its various aspects, as this will promote team work and avoid misunderstandings between individuals and agencies. Physicians, nurses, social workers, teachers and other professionals would meet on common ground in open forum.

A preventive department's significance is evident when one thinks of the large percentage of ward children who, when discharged as cured, return to the hospital after a varying interval of time with a recurrence of the illness. Entirely aside from its humane aspect, it is an extravagant waste of the money that has been expended on the child's care while in the hospital when there is a recurrence of the same disease through failure on the part of the hospital to correct the faulty home conditions that were originally causative. It is the department in the hospital that contributes permanency to all the curative work accomplished in the wards and in the outpatient clinics. Without such a department a large part of the curative work has but fleeting value, a much larger percentage than is recognized. When such a department exists, the number of readmissions will be strikingly reduced and strikingly increased. By this seeming paradox I mean it has been demonstrated that many of the illnesses will not recur if the child is kept under observation, hence a reduction in readmissions. On the other hand, many children are readmitted promptly when the need of hospitalization has been recognized by the field worker or the physician in the health clinic, although overlooked by the parents. It is difficult to prevail on parents to continue to bring back to a curative clinic their child after they believe he is well, but when there is a special department the object of which is to prevent children from becoming sick, parents will be eager to bring their children regularly and as often as the hospital desires.

A distinct division for the prevention of disease would make an ideal teaching center for students of child health. It presents excellent material from which to teach preventive medicine to medical students, both undergraduates and graduates, the fundamentals of public health nursing to pupil and affiliated nurses and the specialized social work essential to a pediatric hospital to social workers.

A comprehensive course in applied child hygiene, the prevention of disease and social medicine should be given to graduate and undergraduate medical students by demonstration and practical work in the health clinic. Sociology, psychology and psychiatry should be funda-

mental studies before entrance to the practice of pediatrics. The instruction of the medical student in the prevention of disease develops his ability to think in a broad way of medical problems, and teaches him to correlate the social and medical facts of a case. The department for the prevention of disease should be a teaching center also for interns, pupil nurses, public health nurses and all workers in children's institutions, such as convalescent homes, foster homes, orphan asylums and day nurseries. A children's hospital, whenever possible, should consummate an affiliation with both an undergraduate and a graduate medical school, and also with a school for social workers. Teaching should be conducted by the hospital staff in the wards, in the outpatient department and in the department for the prevention of disease. By instructing all professional persons interested in children, there may be an ever increasing knowledge of child health possessed by all who have, or will have, the care of children.

The criticism is sometimes made that preventive work is not a hospital's function, but belongs to the municipal division of child hygiene. The answer to this is that municipalities carry on only well established and thoroughly tested health activities, and there is always the need for organizations privately conducted which will carry on experimental work for the advancement of the knowledge of preventive medicine. Among the advantages enjoyed by a department for the prevention of disease in a hospital is the benefit of having at hand the facilities of all the special clinics for the correction of the defects discovered. The ideal health center, public or private, will eventually have to have a complete hospital equipment and be staffed with specialists. A teaching center such as the department for the prevention of disease in a children's hospital is needed for all the various groups of students; but in a city-owned health center such extensive use by private students would not be feasible, and further, the pediatric teachers with university qualifications would not there be available. Health examinations for less than half the preschool children in our cities, who come from homes of limited incomes, is entirely inadequate; yet how strange it is that one repeatedly hears the unfounded cry of duplication, and the faulty argument that hospitals should not do preventive work as it is being done in municipal health centers. I believe that for one case of duplication, there are a thousand other cases neglected. What city covers even remotely the health work needed for its children? Even a hundred years hence, when there may possibly be an adequate number of health centers, it will still be necessary for hospitals to be pioneers in this work, unless the health centers themselves become hospitals in personnel, equipment and budget. Since Gerstenberger's pioneer work in Cleveland, the progress of hospitals in the prevention of disease has not been as rapid as it has merited.

May the hospital of the future need fewer ward beds for sick children, and may these be used chiefly for children requiring special diagnostic procedures! Then the curative outpatient department will be comprised of a large pediatric clinic and many subsidiary clinics, covering all the known specialties. A considerable portion of the hospital will be devoted to a department for the promotion of normal development and growth. It will contain an educational department for health instruction of children and parents, as well as of different professional groups requiring training in child hygiene.

One cannot help commenting on the large number of hospitals claiming full participation in prophylactic medicine, but when one inquires specifically, the usual reply is, "Of course we run a well-baby clinic for teaching normal feeding!" Heaven preserve us! If that is all there is to preventive pediatrics, then there is good reason for calling us by that exalted cognomen, "Baby Feeder." Does not the well child, past infancy, need health examinations? It is a far cry from a hospital that has only a well baby feeding clinic to one that has a complete department for the prevention of disease. The hospital should exert a broad protective attitude toward childhood, for the voice of a children's hospital does have great weight in its community on matters pertaining to the prevention of disease, but as yet it has not raised its voice above a whisper. The fundamental object of a department for the prevention of disease is to build better citizens for the future, and, therefore, the most important work a hospital can do is to keep children well. If so-called preventive measures do prevent, and the evidence that this is so is increasing more and more, how can a hospital, if it is a teaching or a research institution, avoid having a department for the prevention of disease? Much for cure, more for prevention, most for child health!

Are hospitals awake to the fact that the whole country is becoming more and more "child-minded"? The modern children's hospital should cherish philoprogenitiveness and strive more to realize its opportunity as a training school to enrich the social, health and spiritual development of the child, for the child alone can save Humanity.

STILLBIRTHS

ANALYSIS OF THE CAUSES OF DEATH IN 338 CASES AS DETERMINED BY NECROPSY

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The causes of fetal death may be grouped under two main heads: maternal and fetal, but it is difficult to classify them in such a simple manner. A fetus, Holland [1] has stated, becomes an infant, child or baby as soon as it has breathed. The fetus dies when its heart ceases to beat. Ballantyne [2] has suggested that the term stillbirth should be applied if a child is born "still" but with discoverable signs of life, such as a beating heart, and that deadbirth should be applied if life is actually extinct. De Lee [3] feels that the simplest classification would use the two terms synonomously. In this report all births included as stillbirths are those in which the fetus never breathed, even though the heart continued to beat for a few minutes after birth.

This report is based on observations made in 338 necropsies performed on stillborn fetuses examined in the department of pathology at the University of Minnesota from July, 1928, to September, 1930. In order to group the cases accurately, the history of the pregnancy and labor was utilized as well as the postmortem data. Forty-seven of the group were born before the twenty-eighth week of uterogestation; strictly speaking, the fetuses being regarded as nonviable at that time, their births would not be classified as true stillbirths. The cases may be regarded as fairly representative, for they include stillbirths both at hospitals and in homes. They are classified according to the age of the fetus, which is determined by the length in centimeters in accordance with Hasse's rule. Records were incomplete in certain of the necropsy reports; therefore, one group must be listed as age unknown. The primary cause of death is listed and tabulated, but explanation supplementary to these data reveals contributing causes that may have been

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Work done under the direction of Dr. Bell, University of Minnesota.

1. Holland, Eardley: The Causation of Foetal Death, London, His Majesty's Stationery Office, 1922.

2. Ballantyne, J. W.: Registration of Stillbirths, J. Obst. & Gynaec., Brit. Emp. **25**:132 (March) 1914.

3. De Lee, J. B.: Principles and Practice of Obstetrics, ed. 5, Philadelphia, W. B. Saunders & Company, 1928.

potent factors in certain of the cases. The figures shown in the tabulation represent what was found in the given material; no attempt is made to offer a basis for estimation of the causes of stillbirth throughout the country.

Syphilis was the cause of death in 5.32 per cent of the cases. The demonstration of Spirochaeta pallida is, of course, absolute evidence of syphilis. There is a great deal of other evidence, some of great and some of small value. Observations on which a diagnosis of the condition depended in this report were osteochondritis in the ends of the long bones, enlargement of the liver, spleen or both, or demonstration of the organism in certain of the fetal tissues stained by the Levaditi

Causes of Death in 338 Cases of Stillbirth

Cause of Death	Males	Females	Total	Per Cent	Age, Months: Less Than 5	5-6	6-7	7-8	8-9	9-10	10 and More	Unknown
Stillbirth	180	158	338	....	1	10	36	42	43	59	101	46
Syphilis	11	7	18	5.32	..	..	1	3	4	7	...	3
Toxemia of pregnancy	6	9	15	4.42	..	..	1	4	3	3	3	1
Placenta praevia	4	7	11	3.25	..	..	..	..	3	2	5	1
Abruptio placentae	9	3	12	3.55	..	..	..	2	1	4	4	1
Prolapse and compression of cord	4	5	9	2.66	..	..	1	..	1	3	4	..
Prematurity	33	21	54	15.97	1	3	16	12	12	2	..	8
Past maturity	2	2	4	1.18	..	..	..	..	..	..	4	..
Trauma at birth	54	47	101	29.88	..	1	5	5	8	18	61	3
Malformation (congenital)	15	22	37	10.94	..	1	8	7	5	5	3	8
Vaginal bleeding (cause unknown)	2	2	4	1.18	..	..	2	..	..	1	..	1
Difficult labor (cause not given)	..	2	2	0.59	..	..	..	..	..	1	1	..
Asphyxia (cause undetermined)	1	..	1	0.29	..	..	..	..	..	1	..	..
Meningitis (focal)	..	1	1	0.29	..	..	..	..	..	1	..	..
Fetus papyraceous	..	1	1	0.29	..	..	..	..	..	..	..	1
Oligohydramnios	1	..	1	0.29	..	..	..	1	..	..	..	..
Intra-uterine death (macerated)	31	23	54	15.97	..	5	2	7	6	9	9	16
Undetermined	7	6	13	3.84	..	..	..	1	..	2	7	3

method. The maternal Wassermann reaction of the blood was positive in the six cases in which the test was made. The most constant observation was syphilitic osteochondritis, which was present in eleven cases. There were more males than females in the series. In ten cases the bodies were macerated; MacCallum stated that this is often observed. One fetus had multiple congenital anomalies, one had hydrocephalocele, one had a DuBois abscess, one had universal hydrops, and one had hydrops of all the serous cavities. Williams [4] reported 302 fetal deaths at the Johns Hopkins Maternity Hospital between April, 1916, and December, 1919; syphilis was the cause of death in approximately a third of the cases.

Maternal toxemia caused 4.32 per cent of the deaths. The cases may be further subdivided into four cases of eclampsia and eleven cases

4. Williams, J. W.: The Significance of Syphilis in the Prenatal Care and Causation of Fetal Death, Bull. Johns Hopkins Hosp. **31**:141 (May) 1920.

of toxemia, in which two or more of the following conditions occurred: hypertension, albuminuria, disturbances of vision and edema. Labor was frequently premature in cases of toxemia, as is indicated in the tabulation. Fairbairn [5] stated that in eclampsia the fetal mortality is due to toxemia, prematurity, placental abnormalities and injuries from operative intervention. The condition of the placenta is undoubtedly a factor in fetal mortality from toxemia, but it was not examined in the cases under consideration. Three fetuses showed evidence of intracranial trauma. Five of the bodies were macerated, and in one case there was a history of premature rupture of the membranes. At Harper Hospital [6] in Detroit, the most common cause of fetal death in nonviable (before seven months' development) and in premature, but viable. fetuses, was found to be nephritic toxemia. In mature fetuses the most common cause of death was associated with labor and delivery.

As indicated in the table, the fetal mortality in placenta praevia is due no doubt in part to the fact that the accident so frequently occurs while the fetus is premature. In other cases, the fetus perishes from asphyxiation, the result of placental hemorrhage, and occasionally it succumbs in attempts at extraction through an imperfectly dilated cervix. In eight of the cases in this series there was evidence of trauma of birth. The proportion of deaths due to placenta praevia was 3.25 per cent. In four cases (1.18 per cent) vaginal bleeding the cause of which was not given was listed as the cause of death.

Premature separation of the placenta was the cause of death in 3.25 per cent of the cases, and prolapse and compression of the cord was the cause in 2.64 per cent; in both instances death was due to imperfect oxygenation, since the supply of properly aerated blood through the umbilical vessels was partially or completely shut off. De Lee stated that operation for prolapsed cord results in a mortality of from 40 to 50 per cent, and that if nature is left to take its course, it is 80 per cent. Fairbairn feels that the mortality associated with prolapse of the cord is not less than 60 per cent. In three of the cases in this series in which prolapse and compression of the cord had occurred, there was evidence of trauma at birth. Two bodies were macerated.

From the pathologic standpoint, premature fetuses must include two groups: one consisting of fetuses whose death occurred during the period of nonviability, that is, before the twenty-eighth week, and the other consisting of those beyond the twenty-eighth week of development.

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5. Fairbairn, J. S.: Obstetrics and Gynecology Text, New York, Oxford University Press, 1921.

6. Kamperman, George: Fetal Mortalities: An Analytical Study Based on Two Years' Records (1925-1926) at Harper Hospital, Am. J. Obst. & Gynec. **16**: 66 (July) 1928.

Lyon [7] stated: "We should regard stillbirths as those that occur beyond the twenty-eighth week only, and should not be held responsible for the life of the child before the period of viability." In the 338 cases, fifty-four (15.97 per cent) of the births were premature; there was no other obvious primary cause of death. Twenty fetuses were born in the nonviable period. Twenty-six were born in the viable period, and the age of eight could not be calculated because of incomplete records. In two cases the mother had fallen shortly before delivery, and in one case the mother had an appendectomy eight days before delivery. Four of the mothers gave a history of previous abortions, miscarriages, premature labor or stillbirth; in other cases an adequate history was not obtained, so this figure is not of much value. In one case there was history of threatened abortion.

In four of the cases the only attributable cause of death was birth past maturity. The average length of these fetuses was 52.5 cm., and the average calculated duration of pregnancy was ten and a half months. The history of pregnancy and labor was essentially normal. In every instance the duration of pregnancy was calculated from the length of the fetus. Kamperman quoted De Lee as considering birth past maturity a just cause for fetal death.

The deaths due to trauma of birth constituted 29.88 per cent of all the stillbirths. It may be noted that the frequency of trauma increases with age, and that the greatest incidence is at ten months or more. In cases in which the fetus had matured or was past maturity, the size of the fetus was a factor necessitating operative procedures in which trauma is not infrequent. The most common injury at birth was laceration of the falx cerebri, the tentorium cerebelli, or both, with or without intracranial hemorrhage. In four cases there was hemorrhage in the suprarenal glands and in one case the sole evidence of trauma was bilateral hematoma of these glands. Rupture of the liver and hemorrhage from it occurred in three cases, besides intracranial injury. In six cases one or more bones of the skull were fractured.

Beneke's method was employed in opening the skull; that is, two oval windows were removed from either side of the sagittal suture. This exposes the cerebral and cerebellar hemispheres without injury to the falx or sinuses; thus free blood cannot be attributed to faulty technic.

Nineteen deliveries were made by forceps, four by craniotomy, three by cesarean section and nine by version and extraction. In three cases labor was induced, and in two the membranes ruptured three or more days before delivery; in the remaining cases delivery was spontaneous.

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7. Lyon, E. C., Jr.: Study of Still Births Occurring in 4,000 Consecutive Deliveries, Tr. Am. Gynec. Soc. **52**:160, 1928.

Serbin [8] has satisfactorily explained the preponderance of cerebral hemorrhage following delivery by forceps. With the application of the blades the longitudinal diameter of the skull is increased, and there is compensatory shortening of the transverse diameter with undue tension on the falx cerebri and on the tentorium cerebelli, thus producing a tear of the tentorium, the adjacent sinus and veins of Galen.

Chase [9] has noted that if birth occurs prematurely, tentorial splits are relatively more common than if birth occurs at full term. This, he has shown, is partly due to the immaturity of the fibers of the dural septums in cases of premature births. At this time, the blood vessels are delicate, there is an abundance of lymph spaces and the falx and tentorium contain few collagenous fibers or elastic fibrils, being composed chiefly of fibroblasts. Thirty-seven of the births in this series were premature, and six occurred in the nonviable period.

Malformations were the cause of death in 10.94 per cent of the cases of stillbirths. This percentage probably is not an index of the frequency of malformations in stillbirths as a whole. Many of the cases were referred to pathologists by general practitioners who, no doubt knowing the relative infrequency of malformations, made particular efforts to bring such cases to necropsy. In the series of cases at Harper Hospital, previously referred to, malformation was the fourth most common cause of stillbirth as compared to the third most common cause in this report.

There were twenty-one fetuses with anencephaly. Extremely small suprarenal glands were noted in all of these cases. There were seven cases of craniorachischisis, spinorachischisis or both, four cases of meningocele, two of meningo-encephalocele, one of hydrocephalocele and two of multiple congenital anomalies. In one of the last cases, spina bifida, aplasia of the bones of the skull, supernumerary digits, deformity of the aortic valves, contiguity of the spleen and pancreas, bicornate uterus and hypoplasia of the cerebellum were present; in the other, craniorachischisis, aplasia of the abdominal wall, exstrophy of the bladder, bilobate right lung, accessory spleen, defect of the diaphragm, two appendixes, imperforate anus, cystic uterus, deformity of the wall of the thorax and deformity of the left kidney were present. Among the cases in which death was due to syphilis there was one of hydrocephalocele and one of multiple congenital anomalies. In the cases in which death was due to trauma, malformations occurred in three; coarctation of the aorta

8. Serbin, W. B.: Report of 320 Fetal Postmortems at the Chicago Lying-In Hospital, Am. J. Obst. & Gynec. **15**:682 (May) 1928.

9. Chase, W. H.: An Anatomical Study of Subdural Haemorrhage Associated with Tentorial Splitting in the Newborn, Surg., Gynec. & Obst. **36**:31 (July) 1930.

in one, spinorachischisis and meningocele in one, and harelip and cleft palate in one.

In two cases, difficult labor, the nature of which was not given in the records, was the cause of death. It is probable that if detailed histories of labor were available, these cases might well have been placed in another group. In one case death was due to asphyxia, the cause of which was not determined. Focal meningitis was found in one case; in this case the mother had had bronchopneumonia and beginning cardiac decompensation at the time of delivery. Organisms were not demonstrated in smears taken from the involved meninges. There was one instance of papyraceous fetus; the body was macerated at birth and adherent to the placenta. The twin was normal. Oligohydramnios was the cause of death in one case. The mother had intestinal obstruction and acute psychosis at the time of delivery. She gave a history of two miscarriages.

In one group of cases no obvious primary cause of intra-uterine death was found; in all these cases the fetuses were macerated at birth. It seems justifiable to group these deaths separately under the heading of maceration. These cases comprised 15.97 per cent of the whole series and made up the second largest individual group. Although the Levaditi staining fluid was not used on all the macerated fetuses, none exhibited the usual gross characteristics of congenital syphilis. Strachan [10] concluded that maceration is the result of retention of the dead fetus in utero whatever the cause. The bony changes in any macerated fetus bear a resemblance to syphilitic osteochondritis and have to be carefully differentiated. Microscopically, the macerated tissues show autolysis of the cell structures of the various organs, edema of the interstitial tissues and extrusion of erythrocytes. In Strachan's cases the condition associated most frequently with maceration was maternal albuminuria; then followed syphilis, maternal eclampsia and extensive placental infarction, respectively. The necropsy records in our cases do not give sufficient data to determine the cause of maceration. This group might well be classified as not determined, being differentiated only by the presence of maceration.

There were thirteen cases (3.84 per cent) in which the cause of death was not determined. All the fetuses were of viable age. There was no pathologic evidence of fetal disease, injury or malformation. There was no history of difficult or complicated labor, maternal disease or other just cause of fetal death. This formed the sixth largest group (table).

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10. Strachan, G. I.: The Pathology of Foetal Maceration; a Study of Twenty-Four Cases, Brit. M. J. **2**:80 (July 15) 1922.

This report has not been offered for the purpose of forming well fixed conclusions as to causes of stillbirth in all localities. It includes data on a group of subjects most of whom came from a rather extensive metropolitan area, and were referred for postmortem examination by general practitioners and specialists. Several observations, however, are worthy of note: 1. Trauma held a paramount place among the causes of fetal death. 2. Prematurity, from whatever cause, is a potent factor in the cause of stillbirth. 3. There is a large group of cases of macerated and fresh fetuses in which the cause of death has not been determined.

NUMBERS AND TYPES OF ORGANISMS FOUND IN CERTAIN PRODUCTS USED IN INFANT FEEDING

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Interest in certain phases of the bacteriology of powdered milk, and more specifically powdered infant foods of various types, was stimulated largely by the recent work of Hucker and Hucker,[1] who, recognizing the need, made a very extensive study of the numbers and a generalized study of the types of organisms occurring in various brands of infant foods. Their study was undertaken primarily with the aim to establish certain standards for the manufacture and control of such products.

The present investigation was undertaken under the guidance of Dr. E. M. Pickens, head of the department of bacteriology and pathology at the University of Maryland. An effort was made to ascertain the numbers of organisms in the powdered products and to classify them as spore-formers, gelatin liquefiers, chromogens, coli-like and hemolyzers. Special attention was given to detecting the presence of hemolytic streptococci.

REVIEW OF THE LITERATURE

Most of the work reported has dealt with the numbers of organisms found in powdered milk. Great variations in counts have been found, numbers ranging from less than 100 to 5,000,000 per gram of powder. In general, it was found that powder prepared by a roller process gave lower counts than that prepared by the spray process, and that the numbers of organisms in the former could be attributed almost entirely to recontamination after drying, while those found in the powder prepared by a spray process were apt to have survived the drying temperatures. In regard to the effect of storage, Supplee and Ashbaugh[2] concluded

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From the Department of Bacteriology, University of Maryland.

1. Hucker, G. J., and Hucker, Alice M.: The Number and Type of Bacteria in Commercially Prepared Infant Foods, New York State Agric. Exper. Sta. Tech. Bull. 153, 1929; The Sanitary Control of Commercially Prepared Infant Foods, ibid. 154.

2. Supplee, G. C., and Ashbaugh, V. J.: Bacterial Content of Milk Powder, J. Dairy Sc. **5**:216, 1922.

that the bacteria die off and reach a point of constancy after from two to four months, and that the "presence of large numbers of bacteria did not produce any detectable effect on the keeping quality in the presence of a moisture concentration which would admit the powder as a commercial article." Macy [3] found that there was a decided decrease during the first year of storage in most samples prepared by the spray process, while the decrease was not so great, relatively, in the powders prepared by the drum process. Diminution seemed to take place more rapidly after the sealed package had been opened. It was interesting to note the report of a count of 52,000 bacteria per gram on one sample in a sealed can at least twelve years old.

Other workers to be mentioned in this "field of numbers" are Hoffman,[4] Grosso,[5] Rossowicz,[6] Heuppe,[7] Prachfield,[8] Delepine,[9] Coutts,[10] Downs,[11] Stocking,[12] Jephcott, Hunwicke and Ratcliffe,[13] Tillmans and Strohecker [14] and Schrader, Ewing, Korpf and Conn.[15] The last mentioned four workers concluded from their determinations of free ammonia and amino-acids that ammonia increases fairly regularly with

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3. Macy, H.: Some Observations on the Bacterial Content of Dried Milk, J. Dairy Sc. **11**:516, 1928.

4. Hoffman, W.: Werden bei der Herstellung der Trockenmilch nach dem Just-Hatmakerschen Verfahren: Lindertuberkel-Bazillen abgetoetet, Arch. f. Hyg. **59**:216, 1906.

5. Grosso, G.: Bakteriologische Untersuchungen von Trockenmilch, Ztschr. f. Fleisch-u. Milchhyg. **17**:312, 1907.

6. Rossowicz, A.: Untersuchungen über den Bakteriengehalt der Trockenmilch, Ztschr. Landw. Vers. Oester. **11**:719, 1908.

7. Heuppe, F.: Ueber Trockenmilch, Centralbl. f. Bakt. **64**:34, 1912.

8. Prachfield, F.: Bakteriologische Untersuchungen einiger Trockenmilch Präparate, Molkerei-Ztg. **18**:2, 1908.

9. Delepine, S.: Report to the Local Governing Board upon the Effects of Certain Condensing and Drying Processes Used in the Preservation of Milk upon Its Bacterial Content, Rep. Local Gov. Board Pub. Health and Medical Subjects, Food Rep. 21, London, 1914.

10. Coutts, F. J. H.: Upon an Inquiry as to the Dried Milks with Special Reference to Their Use in Infant Feeding, Rep. Local Gov. Board Pub. Health and Medical Subjects, Food Rep. 24, London, 1920.

11. Downs, P. A.: Bacterial Flora of Milk Powder, Presented as Thesis for Doctorate in Cornell University, 1920.

12. Stocking, W. A.: Manual of Milk Products, New York, The Macmillan Company, 1917.

13. Jephcott, H.; Hunwicke, R. F., and Ratcliffe, N.: The Attainment of Bacterial Purity in the Manufacture of Dried Milk, Proc. World's Dairy Cong. **2**: 1265, 1923.

14. Tillmans, J., and Strohecker, R.: Ueber Krause Milchpulver, Ztschr. f. Untersuch. d. Nahrungs-u. Genussmittel. **47**:377, 1924.

15. Schrader, J. H.; Ewing, C. L.; Korpf, F. A., and Conn, Lillian W.: Sanitary Quality of Some Commercial Milk Powders, Am. J. Hyg. **8**:386, 1928.

the direct bacterial counts, whereas the amino-acids did not seem to have such a relation. Some idea of the bacterial content of the milk before drying may thus be obtained from an estimation of the ammonia content of the dried product.

Not much work has been done on the types of organisms found in powdered milk. Practically all of the few workers reporting on this agree in finding spore-formers, staphylococci, sarcinae, a few streptococci, yeasts and molds.

Macy [3] noted a predominance of small subsurface colonies resembling those of Streptococcus lactis on plates prepared from high count samples of dried milk. The flora in many plates resembled closely that of freshly drawn milk. The majority of reconstituted milks, when allowed to stand in the refrigerator for two weeks, showed acid coagulation and peptonization and sometimes extensive gas.

Hunwicke and Jephcott [16] claimed that the roller process of drying milk is capable of destroying all nonspore-formers.

Most of the work on pathogenic organisms in powdered milk has been done to determine the presence of the tubercle bacillus. Carre,[17] Martel,[18] Hoffman,[4] Schrader, Ewing, Korpf and Conn,[15] Coutts,[10] Klein,[19] and Hunwicke and Jephcott [16] found no evidence of the presence or survival of the tubercle organism in powdered milk. Delepine,[9] however, found the organism capable of surviving the roller process of drying, and able to produce the disease in guinea-pigs inoculated subcutaneously. The course of the disease was slower than that produced by inoculating the same amount of tuberculous milk not previously dried.

Only one group of workers [15] reported finding the B. coli-type of organisms in powdered milk. The powder they studied was subject to great contamination, having been purchased loose from open containers. Klein,[19] experimenting with milk inoculated with B. coli, B. typhosus, diphtheria bacillus and a mixture of Staphylococcus aureus and B. prodigiosus, found that all these organisms were destroyed by the Eckenberg roller process. From their own experiments and a review of available literature, Supplee and Bixby [20] concluded that the tubercle bacillus, B. typhosus, B. diphtheriae, Staph. aureus, Staph. epidermidis, Strep. mastiditis, the Morgan dysentery bacillus,

16. Hunwicke, R. F., and Jephcott, H.: The Destruction of Bacteria in the Roller Process of Milk Drying, J. Dairy Sc. **8**:206, 1925.

17. Carre, H.: Soc. cent. de méd. vét., 1910, p. 556.

18. Martel, H.: Soc. cent. de méd. vét., 1910, p. 563.

19. Klein, quoted by Coutts, F. J. H.: Rep. Local Gov. Board Pub. Health and Medical Subjects, Food Rep. 24, London, 1920.

20. Supplee, G. C., and Bixby, E. M.: The Bacteriology of Dry Milk with Particular Reference to That Made by the Just Process, Am. J. Dis. Child. **37**: 1016 (May) 1929.

the green-producing enterococcus and many saprophytes were destroyed by the Just roller process of drying milk.

Very few experiments have been performed in an attempt to ascertain the presence of hemolytic streptococci. Dick and Dick,[21] undertaking an investigation in connection with the study of an epidemic of enteritis, found as many as 30,000 green-producing streptococci in powdered protein milk and 700 hemolytic streptococci in one sample of the same milk. In a later article,[22] the possibility of tracing the epidemic to the powdered milk is discussed.

Hucker and Hucker,[23] in an examination of 200 samples of prepared infant foods, found no appreciable numbers of hemolytic or viridans types of streptococci.

Sherman, in the work reported by Ashton, Stringfield and Martin,[24] found a count of 14,000 colonies per gram of powder, showing beta hemolysis on meat infusion agar plus 0.5 per cent defibrinated horse blood. Forty cultures of these colonies were selected for study. All survived heating at 60 C. for thirty minutes, and gave reactions characteristic of the bovine types. From his studies, Sherman concluded that the organisms were not of the human pathogenic type.

EXPERIMENTAL METHODS

Twenty different kinds of infant foods were used in this study. These included powdered whole milks, powdered milks modified to suit the needs of various infants, powdered products for use in modifying cow's milk to render it more suitable for infant feeding and certain synthetic compounds designed to provide a complete nutrient. The products were purchased, unopened, from local drug stores as they were needed for study during the months of January, February, March and April, 1930.

Before opening, the top and sides of the can were flamed. In an effort to secure a representative sample, the contents of each can were mixed, care being taken to avoid contamination, by removing with a sterile spatula part of the powder into a sterile, wide-mouthed, Erlenmeyer flask with a capacity of from 300 to 500 cc. With the exception of the first ten cans studied, two different samples were used from each can, one sample taken from the flask and one from the can itself. Five and six samples were taken from each of the first ten cans studied. One gram samples were weighed aseptically on sterile filter paper and suspended in 10 cc. of sterile water, previously heated to between 40 and 45 C. in 125 cc. flasks. After

21. Dick, G. F., and Dick, Gladys H.: The Bacteria of Dried Powdered Milk Preparations Used in Infant Feeding, Am. J. Dis. Child. **34**:1040 (Dec.) 1927.

22. Dick, G. F., and Dick, Gladys H.: The Etiology of an Epidemic of Enteritis Associated with Mastoiditis in Infants, Am. J. Dis. Child. **35**:955 (June) 1928.

23. Hucker, G. J., and Hucker, Alice M.: Organisms Associated with Commercially Prepared Infant Foods, Am. J. Dis. Child. **38**:310 (Aug.) 1929.

24. Ashton, L. O.; Stringfield, O. L., and Martin, C. W.: A Study of the Routine Use of Powdered Whole Milk in Infant Feeding, Arch. Pediat. **46**:75, 1929.

thorough shaking for about five minutes, the flasks were again held in a water bath at 45 C. for ten minutes. This aided reconstitution without killing any of the organisms that might be present. Care was taken to break up, as far as possible, all lumps of powder.

The first 1:10 dilution is not quite representative of the reconstituted product, which usually is a 1:7 or 1:8 dilution. The dilutions used for plating in most cases were 1:10, 1:50 and 1:500, using 1 cc. quantities of each. Four different sets of plates were poured for each sample, four kinds of mediums being used. All plates were incubated at 37 C. for forty-eight hours, except gelatin plates, which were incubated at 20 C. for three days, after which time counts were made.

For total counts, counts of spore-formers and chromogens and for a general idea of the types of organisms present, standard [25] beef-infusion agar was used.

Examination for coli type colonies was made on Endo's agar, beef-infusion being used in preparing the mediums. Each batch of medium that was made was tested before use for its efficiency in differentiating coli by plating a mixture of a known culture of B. coli and some other organism.

Gelatin liquefiers were counted on plates poured with beef-infusion gelatin mediums. In cases in which liquefaction was so rapid and extensive that an accurate count was not possible, an approximation of the colonies was obtained by estimating and averaging the counts on all three dilutions. In some instances liquefaction was so rapid and complete that counts were impossible.

Hemolyzing colonies were counted on a medium containing, per liter of beef-infusion, the following substance: agar, 15 Gm.; sodium chloride, 5 Gm., and Difco peptone, 5 Gm. The reaction was adjusted to p_H 7. This medium was tubed in quantities of 10 cc., and, previous to plating, 1 cc. of sterile citrated cow's blood was added to each tube and thoroughly mixed. The blood was tested for sterility at each plating. Plates selected for counting were those on which occurred the greatest numbers of hemolyzing colonies, provided there was not too much spreading and fusion of hemolysis to prevent accuracy. Hemolyzing colonies were classed as 1, 2, 3, 4 or 5, according to the size of the colony and the zone of hemolysis around it. All hemolyzers falling in classes 4 and 5 proved to be spore-formers, and the majority in class 3 were spore-formers. Those in class 1 and class 2 were mostly cocci, a few rods and streptococci.

There was not sufficient time to identify all the bacteria found in each sample. However, organisms from representative colonies were picked from each set of plates and their morphology studied. In this way, an estimation of the types present and their relative proportions in each sample was obtained. A few of the most interesting organisms were selected for special study.

All counts are recorded as numbers of organisms per gram of powder. After these results were obtained, plates were kept for about a week and examined again, any changes as to chromogenesis and mold growth being noted.

COMMENT

Nine milk modifiers were selected for study. These products are used in cow's milk to make it more adaptable for infant feeding.

Milk modifier A was found to contain, chiefly, spore-bearing organisms, though a few coccus forms were noted. Modifier B also con-

25. Standard Methods of Milk Analysis, ed. 5, New York, American Public Health Association, 1928.

tained practically all spore-formers. The few colonies in modifier C were streptococci in fairly long chains. These colonies on the blood agar plates were rather large, smooth and egg-shaped, and appeared bluish under the low power objective of the microscope. They produced a green zone around them about equal in width to the diameter of the colony. After about a week, hemolysis, to a slight extent, was noted in a few cases.

Modifier D contained largely spore-formers. Agar plates poured from modifier E contained large, flat, transparent yellow colonies that appeared to be composed of short, thin rods in pairs. Spore-formation was uncertain.

Modifier F, besides spore-formers, contained a few short rods. The poor water-solubility of this and a few other products made it very difficult to count the colonies, since the particles were hard to differentiate.

Modifier G was the only product studied in tablet form. It was especially interesting to note that there was a decided difference in the counts among the individual tablets, as well as between different cans of the same product. This difference in parts of a can as well as in separate cans was noted also in other products. The flora of each can and each product was fairly uniform, however.

The first can of "G" studied contained rather few spore-formers and short rods. Plates from the second and third cans attracted attention because of the relatively large numbers of colonies, and the fact that when the lid of the petri dish was raised, the odor of ammonia was detected. Sterile litmus milk was inoculated with parts of tablets of the product. An appreciable amount of gas formation occurred in twenty-four hours, with rapid peptonization of the milk.

Modifier H showed mostly spore-formers, as did the other products previously described. Especially in the first dilution plates from this product, which contained more of the powder, were clear areas noted around the colonies. It is thought that this might be indicative of proteolytic bacteria, since milk agar plates, made by adding 10 per cent of sterile milk to nutrient agar, have been used to detect proteolytic bacteria in milk. The limitations of this method, however, are pointed out by Frazier and Rupp.[26] The phenomenon of clear areas around colonies was noted in other instances, also. In some cases the dissolving of the particles was so rapid that the whole plate was clear within twenty-four hours.

Modifier I contained micrococci, short rods and yeast.

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26. Frazier, W. C., and Rupp, P.: Studies on the Proteolytic Bacteria of Milk, J. Bact. **16**:57, 1928.

Lactic acid whole milk J contained mostly streptococci and a number of yellow cocci. Blood plates from can 1 showed colonies that first produced a green area around them, and then partial hemolysis occurred. In these cases there was a band of corpuscles remaining around the colony and then a clear zone. The organisms proved to be streptococci, but, as the colonies did not resemble the typical viridans type, their identity as such was doubtful. Can 2 showed the same greenish discoloration of the corpuscles about the colonies, but hemolysis did not occur. Can 3, however, contained streptococci and diplococci the colonies of which were of the beta hemolytic type (classification of Smith and Brown[27]). A smooth curd was formed in sterile milk inoculated with the organism.

One can of lactic acid whole milk K also contained colonies of about this same type, streptococci producing a green zone about the colony.

Product L, a synthetic compound adapted to human milk, contained a relatively large number of hemolytic diplococci in all three cans studied. In one of these cans the diplococci showed a tendency to chain formation. Some of the colonies had a band of corpuscles around them and then the clear zone, while others showed merely the zone of hemolysis. All these colonies are classed as number 1 hemolyzers. The yellow chromogens, which were rather numerous, were very delicate rods, and, in some cases, diplococci.

All three cans of product M, a modified milk, seemed to contain a pure culture of streptococci, occurring in pairs, with about six or eight organisms in a chain. The colonies were smooth, elliptic and mostly subsurface. Some of these produced the green discoloration of the blood corpuscles on the blood agar plates, others a clear zone. Some, when examined under the microscope, showed a clear zone, then a ring of corpuscles and then a second less distinct hemolytic zone. The organisms produced a cloudy growth in plain nutrient broth (beef infusion) and a very soft, acid curd in litmus milk.

Modified milk N contained mostly spore-formers. Modified milk O, besides the spore-formers, contained a few big coccus forms and an occasional streptococcus. Protein milk P showed a few micrococci, some diplococci and some slightly curved rods.

Plates poured from product Q, a milk food, contained a number of yellow cocci, streptococci and a few yeasts and sarcinae. None of the streptococci were hemolytic, however. Powdered milk R contained, besides spore-formers, a few rods and staphylococci.

Powdered milk S contained rather large numbers of typical viridans and beta hemolytic streptococci. The colonies from can 1 were exceedingly small, most of them of pinpoint size. The viridans colonies were

27. Smith, T., and Brown, J. H.: J. M. Research **31**:467, 1914.

recognized by the zone of methemoglobinized cells inside the hemolytic zone. The beta hemolytic colonies showed a sharp, clear zone of hemolysis around the colony about equal in width to the diameter of the colony. Most of them were smooth colonies, though some of the rough variety were noted. The organisms were gram-positive. All of them were diplococci, chained usually in groups of four and six. They grew very poorly in plain broth. In litmus milk a smooth curd was formed with the production of acid. Gorini [28] has suggested that two types of streptococci may be distinguished according to their reactions in milk. To group 1 belong most of the saprophytic organisms, which

Average Counts of Three Cans for Each Product Studied *

		Number of Colonies per Gram of Powder											
							Hemolyzing Colonies, Class						
Product		Total Count on Standard Ager	Spore Formers	Gelatin Liquefiers	Chromogens	Coli	1	2	3	4	5	Total	Molds
Milk modifier	A	5746	4834	2569	0	0	0	153	822	142	342	1459	0
Milk modifier	B	32517	29117	3985	0	0	0	100	5400	2250	2033	9783	10
Milk modifier	C	37	13	0	2	0	0	0	0	0	0	0	2
Milk modifier	D	31750	29958	2545	0	0	0	333	1583	1858	4558	8332	17
Milk modifier	E	795	638	12	315	0	0	0	0	3	5	8	31
Milk modifier	F	516	372	213	0	0	0	0	2	15	87	104	100
Milk modifier	G	26833	10083	3166	83	0	0	0	58	7206	0	7264	175
Milk modifier	H	1225	1041	80	0	0	5	7	117	194	124	447	0
Milk modifier	I	72	7	20	28	0	0	2	0	4	2	8	7
Lactic acid whole milk	J	5975	80	20	244	0	582	0	48	3	7	640	15
Lactic acid whole milk	K	2625	1342	400	342	0	117	0	150	245	210	722	37
Synthetic compound	L	21622	2830	286	2855	0	10708	330	122	36	125	11321	31
Modified milk	M	12154	466	273	308	0	2342	93	218	70	75	2798	12
Modified milk	N	5646	4958	210	33	0	0	66	705	37	132	940	41
Modified milk	O	8497	7658	3855	0	0	37	54	1642	1479	921	4133	0
Protein milk	P	350	43	19	0	0	0	0	2	22	0	24	42
Milk food	Q	6150	358	153	1858	0	3	100	52	33	68	256	47
Powdered milk	R	1209	1007	58	0	0	2	0	20	42	50	114	0
Powdered milk	S	98025	1016	458	8900	0	19305	0	190	166	133	19794	0
Powdered milk	T	526	65	47	25	0	0	175	0	1	0	176	227

* The figures on the chart were obtained by computation, averaging the counts on all samples taken from each can, and from all three cans of each product studied.

rapidly produce a firm coagulum in the milk, while to group 2, which slowly and irregularly produce a flocculent coagulum, belong most of the pathogenic streptococci.

A 1:10 dilution of the powder was incubated at 55 C. for twenty-four hours and then plated on blood agar. Only about 400 hemolytic streptococci remained alive or retained their power of hemolyzing. Another interesting fact noted was that there were never as many hemolyzing colonies, proportionately, on the higher dilution plates as on the lower. This was probably due to the fact that the organisms grew better in a milk medium.

28. Gorini, C.: Sur les streptocoques acidoprotéolytiques, Compt. rend. Soc. de biol. **95**:79, 1926.

Two guinea-pigs, inoculated intraperitoneally and subcutaneously, respectively, with a washed agar culture of the hemolytic streptococci were apparently unaffected.

Two other cans of "S" showed hemolytic streptococci of the beta type, also, but the colonies were not as numerous or as small as in can 1.

Plates from powdered whole milk T showed diplococci and spore-forming rods. One can contained organisms that proved to be hemolytic streptococci. The colonies were rather large, smooth and elliptic.

No B. coli types were encountered in any of the products. These findings agree with those of most workers.

Most of the products contained molds. The mucor and aspergillus varieties were recognized, among which were noted Mucor mucido, Aspergillus flavis and Aspergillus glaucus. Most of the molds were of the more or less common types, and have little significance in the products except as evidence of contamination.

SUMMARY

Of twenty brands of powdered infant foods studied, average total colony counts made on standard agar ranged from 37 to 98,000 per gram after forty-eight hours' incubation at 37 C.

The majority of organisms found were spore-formers, ranging from 7 to 29,900 per gram, though micrococci, streptococci, nonspore-forming rods and a few sarcinae, yeast and molds were found. Gelatin liquefiers varied from 0 to 34,000, and the number of chromogens, from 0 to 8,900 per gram. No colon type colonies were noted.

Average total counts of hemolyzing colonies were from 0 to 19,800 per gram, though individual counts as high as 160,000 were obtained. Viridans and beta hemolytic streptococci were found in five different products, and their presence was questionable in two others. In one product these organisms numbered as high as 160,000 per gram. Cultures obtained from this sample were not pathogenic for guinea-pigs.

STOVARSOL IN THE TREATMENT OF SYPHILIS IN INFANTS AND IN CHILDREN

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If the oral treatment for syphilis were as efficient or more efficient than the other modes of treatment, it would have many incidental advantages. Stovarsol,[1] spirocid or acetarsone—they are the same product—administered by mouth has given such superior results that we decided to test it in our clinic.

Since 1922 in animal experiments and 1924 clinically, the French have used stovarsol. Later it has been used extensively with great favor in Germany, Austria, Hungary, Czecho-Slovakia and Poland. In this country, Cregor and Gastineau [2] tried it for the treatment of adults and compared its efficiency with that of neoarsphenamine.

Oral treatment offers special advantages in infants and children. Any one who has had experience in the treatment of syphilitic children knows with what difficulty and sacrifice a social worker, a bread winner, a busy mother or a caretaker brings a child to the clinic weekly over a long period. When acute symptoms have disappeared, persistent importunity is often required to get the child treated. As a consequence, treatment is often irregular or entirely discontinued.

A point stressed by Paul von Kiss [3] is that visits of infants to the dispensary should be minimized to protect them as far as possible from exposure to severe weather and from children with colds or other contagious disease. Older children, while more resistant, are entitled to the same consideration. It should not be forgotten that occasionally it is desirable that an older child should not know that he is being treated for syphilis. Injections are apt to be a more telltale procedure. There are children who dread injections so much that they think about them at night, and some have a storm of fear before being treated. Others must always be forced and held while treatment is being given.

Stovarsol is an odorless, white tablet tasting like acetylsalicylic acid and is easily soluble in water or milk. None of the children in this

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From the Syphilis Clinic of the Children's Memorial Hospital, Chicago.

1. The stovarsol for this study was supplied by Merck & Company.

2. Cregor, Frank W., and Gastineau, Frank M.: Stovarsol in the Treatment of Syphilis, Arch. Dermat. & Syph. **15**:43 (Jan.) 1927.

3. von Kiss, Paul: Der heutige Stand der peroralen Behandlung der Lues congenita, Jahrb. f. Kinderh. **126**:211 (Jan.) 1930.

series has complained when taking it. It is marketed in 0.25 and 0.1 Gm. tablets. Chemically, it is an acetyl-4 oxy-3-aminophenylarsenic acid preparation and is similar to arsphenamine, containing about 27 per cent of arsenic.

We began this study in March, 1930, and in the beginning patterned our dosage after that of Tuscherer [4] and von Kiss.[3] After Jan. 1, 1931, we followed that of Alois Bratusch-Marrain,[5] who seemed to have worked out a better system based on weight and clinical experiment. His dosage applies to infants, but he has the impression that the same basis of dosage holds for older children. He says, however, that in syphilis of the central nervous system larger doses give a better result. His system of dosage is as follows: For seven days, 0.005 Gm. of stovarsol per kilogram of body weight is given daily; for seven days, 0.01 Gm.; for seven days, 0.015 Gm., and for forty-two days, 0.02 Gm. A rest period of from four to six weeks follows this course of treatment. The aforementioned courses and rest periods are repeated until the serologic tests are negative and three times thereafter. Then a rest period of six months is given, followed by one more course. Bratusch-Marrain thinks that the best dosage is from 0.01 to 0.02 Gm. per kilogram of body weight, that smaller doses have no effect, and that larger doses offer no advantage.

In all, forty-one children were given stovarsol. Twelve of them had previously received other treatment. Nine infants in the first year have been under treatment with stovarsol for a full year; all of them are clinically and serologically normal. It is likely that this 100 per cent negative record might not occur with a larger series. We hope to determine this fact with more cases. However, the result is in marked contrast to that obtained in thirty-four cases in which the treatment was begun in the first year and was continued for a year or more by the old method in which sulpharsphenamine and mercury were used. Nine, or 26 per cent, of the latter group are Wassermann-fast, and eight of the remainder of this group were treated between one and two years, ten were treated for two years, and four for more than three years. Bratusch-Marrain [5] also reported that the clinical and serologic results with stovarsol were much superior to those of the old type of treatment.

Six of the nine infants treated with stovarsol were markedly syphilitic. Their response to stovarsol was prompt, and in a few weeks their development was like that of a normal child. All infants were given cod liver oil and optimum general care and feeding as far as is possible with ambulatory patients. There was the advantage of excel-

4. Tuscherer, J.: Zur Behandlung der Lues congenita mit Spirozid, Monatschr. f. Kinderh. **45**:63 (Sept.) 1929.

5. Bratusch-Marrain, Alois: Wert und Durchführung der Spirocidbehandlung der Syphilis im Kindesalter, Arch. f. Kinderh. **92**:26 (Nov. 28) 1930.

lent social service and nursing supervision. As observed by others using stovarsol and other arsenicals, the pathologic conditions of the skin, mucous membranes and bones disappeared earliest, namely, in from two to three weeks. Later, the enlargement of the spleen and liver yielded to treatment.

Following are three examples of cases from this group of infants.

REPORT OF CASES

A white boy, aged 7 weeks, when first seen had snuffles, syphilitic facies, desquamating, infiltrated palms and soles and infiltration of the regions of the forehead, eyebrows and mouth. All the finger-nails and toe-nails were lost. The spleen was felt one fingerbreadth below the costal arch. The Wassermann and Kahn tests were negative four months following the beginning of treatment. The general development had been excellent, and the patient walked at 11 months.

A white boy, aged 2½ weeks, when first seen showed a nose filled with a bloody discharge, marked snuffles, eczemato-impetiginous syphilid about the mouth, tense fontanel, retraction of the ribs with inspirations, a spleen on a level with the umbilicus, and marked infiltration and desquamation of the palms and soles. The Wassermann and Kahn tests were negative after seven months of treatment, and the general condition and development were very good. At the time of writing, the patient had been under treatment for more than one year.

A colored boy, 2 months of age when first seen, had marked osteochondritis and epiphysitis; he cried when moved. On palpation epitrochlear nodes were felt to be enlarged (2 plus); snuffles was marked, and the spleen was felt two fingerbreadths below the costal arch. Serologic tests were negative after six months of treatment and remained negative for about one year. The child had walked "holding on" since the age of 10 months. At 10 months, the weight was 20 pounds (9,000 Gm.).

Six children above 1 year of age when first seen received no form of treatment other than stovarsol for one year. Three still give serologically positive reactions at the time this article was written. Fifty-seven, or 50 per cent, of the 114 patients treated by the old method with sulpharsphenamine and mercury, gave positive reactions at the end of one year of treatment.

Twelve of the remaining patients had previously received other forms of treatment, and stovarsol was given not only because of its greater efficiency and because I wished to test it, but because it made regular treatment possible. For example, in one case the mother was pregnant and had two other small children to care for beside the 14 months old patient. In two cases the children lived in another state where it was difficult for them to be treated. After beginning their treatment, prescriptions were given for further treatment and the mother brings the children to the clinic monthly. This plan has worked well, and these children have made remarkably good gains in health and in general development.

A girl, aged 5 years and 5 months, underdeveloped, had a saddle nose, large frontal veins, rhagades, large epitrochlear nodes, carious and crumbly teeth and saber-shin on the left. The Wassermann and Kahn reactions were 4 plus. Examination of the eyes made by Dr. R. Gamble disclosed nystagmus of the ocular type, typical granular pepper-and-salt appearance of each retina, with definite atrophy in each macula, and moderate atrophy of the optic nerves. The patient gained 4 pounds (1,814.37 Gm.) the first month of treatment and stopped wetting the bed shortly afterward. At the time of writing, she has been treated for one and a half years. Nystagmus has disappeared and the vision of the right eye is 20/70, and of the left 20/100. She is in the first grade at school and reads satisfactorily. The Wassermann reaction is 2 plus and the Kahn reaction, 4 plus.

Two patients had condylomas of the anus. One, a white girl, 2 years old, who had never been treated, had a syphilitic facies and an impetiginous syphilid near the right corner of the mouth, which had been present for months. The condylomas measured 3 by 2 cm. on either side of the anus. After two weeks of treatment, the lesions of the face and anus were gone. After one year of treatment, the serologic tests were still positive. However, the general development was good, and there was no clinical evidence of active syphilis.

The second patient with condylomas, a colored boy, aged 3 years and 9 months, showed no other condition suggestive of syphilis. The Wassermann and Kahn reactions were 4 plus. In this case also, the condylomas were completely resolved in two weeks. At the time of writing, he has been treated for four months. The results of serologic tests are the same as before treatment was begun, though in this case cooperation is not reliable.

A girl, 9 months old, had snuffles when first seen, which are still present at the time of writing. There was marked pallor, square head with overhanging brow, saddle nose, elevated fontanel and scaling in the region of the eyebrows. There was also the following unusual condition: the fingers were tightly clenched in the palms and could neither be voluntarily extended nor completely extended by manipulation, and the muscles of the dorsa of the hands appeared atrophied. She was given treatment with stovarsol and hematinics, and, under orthopedic direction, the hands were massaged and treated twice a week by a visiting nurse and daily by the mother. At the time of writing, the fingers can be extended and used normally by the child, and the dorsa of the hands do not appear wasted. The serologic tests are still positive, but the color and the general condition are very good.

A boy, 4 months of age, poorly nourished and with extensive furunculosis when first seen, had been under treatment for about three months. He was doing well when he contracted pertussis followed by bronchopneumonia and death. Another boy, 4 months old, had been under treatment about three weeks when he contracted an infection of the upper respiratory tract with bilateral purulent otitis media and enteritis, ending fatally.

Stovarsol gave satisfactory results in the other cases, but they are not reported here as there were no unusual findings, and the patients had not been under treatment for one year.

Reactions to stovarsol occurred rarely. A patient, 9 months old, was given one fourth of a 0.25 Gm. tablet. The temperature rose to 104 F. rectally. She was admitted to the hospital, and nothing abnormal other than the temperature was noted. She was discharged the next day with a normal temperature. The day following discharge the mother gave her another dose of stovarsol through a misunderstanding, and again the temperature rose rapidly to 103 F. One-half grain (0.0324 Gm.) of mercury with chalk was given three times a day for two

weeks, then stovarsol was given again, this time without reaction. At the time of writing, the patient has been under treatment with stovarsol for five months. In this patient the febrile reaction may have been due to stovarsol.

In a girl, 5 years and 5 months old, who had received treatment for two months, an erythema of the dorsal surfaces of the upper extremities and, to a lesser degree, of the lower extremities developed. Treatment was discontinued for a week and the rash disappeared. Treatment was resumed, and the rash did not reappear. This was the only patient with a rash, which was in all probability due to stovarsol.

In a girl of 12 years, with normal urine, erythema developed following the administration of sulpharsphenamine, and later a bismuth line occurred when the usual doses of bismuth were given. Stovarsol was then given without reaction, and the patient did well under this treatment.

One girl, 6 weeks old, presented a bloody, snuffly discharge dripping from the nose; the head was retracted, and saddle nose, markedly syphilitic facies, glazed and scaling palms and soles and a maculopapular rash were noted. The liver was felt three fingerbreadths below the costal arch and the spleen, two fingerbreadths below the costal arch. There were ulcerations and thrush in the mouth. The patient was given one-fourth tablet of stovarsol. She died the next day at her home. In such severe cases of syphilis, patients die after the slightest provocation, and it is likely that the administration of stovarsol had no connection with this death. On a former occasion a patient with a similar case with less severe involvement of the mucous membranes but with marked visceral syphilis died in the hospital following the administration of a small enema; she had received no antisyphilitic treatment. Another infant with marked visceral syphilis died at home, and this child was being treated with weekly injections of $\frac{1}{200}$ grain (0.000324 Gm.) of mercuric chloride. However, in treating such a patient with such a severe case of syphilis, I think that it would be well in the beginning to use some mild antisyphilitic treatment such as one-half grain of mercury and chalk, U.S.P., given by mouth twice a day, or mercurial rubbings for a few days before an arsenical is used.

Loss of appetite, vomiting or diarrhea was not noted in any of our patients.

It is interesting to note that Soldin and Lesser,[6] comparing the mortality of patients under treatment with the old method from 1919 to 1924, with the mortality following treatment with stovarsol from 1924 to 1928, noted a much lower mortality with the latter. It must also be said that Soldin and Lesser used a much larger dosage of stovarsol even from the beginning of treatment than Bratusch-Marrain.[5] Bratusch-Marrain reported the occurrence of a Jarish-Herxheimer reaction in one of his forty-seven cases.

In the older methods of treating syphilis, it always seemed advisable to use first one metal, and, as the tissues became resistant to the metal used, to employ another. In our experience the use of stovarsol

6. Soldin, M., and Lesser, F.: Stovarsol in Syphilis of Infants, Deutsche med. Wchnschr. **51**:991, 1925; Weitere Erfahrungen mit Spirozid der Saüglingssyphilis, ibid. **54**:958, 1928.

has been so successful that this has not been done. It would seem, however, that if a resistant case should occur mercurial rubbings could be used alternately with stovarsol, and if it were desired to give injections, one of the reliable bismuth preparations could be used. Iodides could also be used when indicated. It would appear, however, that in the majority of cases the condition responds satisfactorily to stovarsol when given as previously directed.

CONCLUSIONS

1. In forty-one cases of congenital syphilis in which treatment was given by mouth, stovarsol gave satisfactory results. In nine the treatment was begun during the first year and continued for a year or more; serologic reversal was obtained in all cases, and clinical results were excellent.

2. Of six patients who were more than 1 year of age when treatment was begun and in whom it was continued for a year or more, serologic tests became negative in only three though clinical results in all of them were excellent.

3. The remaining cases were not reported as a group since the patients were not under treatment for a period of a year. Clinical improvement occurred in all patients. The serologic tests were reversed or influenced in most cases.

4. Few reactions occurred.

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ACID-BASE BALANCE OF NEW-BORN INFANTS

II. CONSIDERATION OF THE LOW ALKALINE RESERVE OF NORMAL NEW-BORN INFANTS

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The acid-base equilibrium of new-born infants has proved a fertile field for research. Interesting differences exist between the new-born infant and the adult. In the first paper of this series, Hoag and Kiser [1] showed that the serum of the new-born infant has a lower carbon dioxide content and a higher chloride content than that of the normal adult. Other authors have reported similar decreases in the carbon dioxide content of the serum. Kane and Kreiselman [2] found an average value of 47.7 per cent by volume for the carbon dioxide content in the cord blood of forty-seven infants. Leenhard and Chaptal [3] demonstrated that there is a decrease in the bicarbonate of the blood of young infants. Halfer [4] found a latent acidosis in the new-born infant as manifested by a decrease in the carbon dioxide content of the blood, which usually persisted during the first two weeks of life.

A similar alteration of the acid-base equilibrium was predicted by Yllpö in 1916.[5] He employed the unusual method of estimating the difference between the p_H of blood as drawn and the p_H of blood from which the carbon dioxide had been extracted by evacuation. In normal adults, this difference is 1.00, which he expressed as 100 per cent. In new-born infants, he found the difference to be only 60 per cent, and he argued that the cause must have been an accumulation of nonvolatile

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1. Hoag, Lynne A., and Kiser, W. H., Jr.: Acid-Base Equilibrium of New-Born Infants: I. Normal Standards, Am. J. Dis. Child. **41**:1054 (May) 1931.

2. Kane, Howard F., and Kreiselman, Joseph: The CO_2 Content of the Blood in the New-Born: A Preliminary Report, Am. J. Obst. & Gynec. **20**:826, 1930.

3. Leenhard, E., and Chaptal, J.: La réserve alcaline du sang nourrisson et de l'enfant: sa valeur et ses variations physiologiques, Rev. franç. de pédiat. **3**:641, 1927.

4. Halfer, G.: Untersuchungen über das Verhalten der Alkalireserve bei gesunden und kranken Kindern, Klin. Wchnschr. **9**:501, 1930.

5. Yllpö, A.: Neugeborenen; Hunger; und Intoxicationsacidosis in ihren Beziehungen zueinander, Ztschr. f. Kinderh. **14**:268, 1916.

acids at the expense of the carbon dioxide in the blood. This method has been criticized by Hasselbalch,[6] who expressed the belief that these differences are due to variations in the hemoglobin content of the whole blood and do not necessarily indicate the presence of acidosis. However, Yllpö [7] repeated his work, using serum instead of whole blood, and confirmed his previous conclusion that the new-born infant has a tendency toward acidosis, or, as he calls it, an "acidotic constitution."

These reports indicate an alteration of the alkali reserve during early life; they suggest a comprehensive investigation of the status of the acid-base system in new-born infants. A complete examination, however, would entail analyses for all components of the system, necessitating larger quantities of blood than one would be justified in withdrawing from small infants. This investigation is, therefore, confined to the determination of the p_H, carbon dioxide, chloride, protein and total base of the serum, these being the most important constituents. Bicarbonate, chloride and protein constitute normally about 96 per cent of the anions combined with the fixed base of the serum. Variations in the remaining fraction of the anions would not be expected to influence markedly the acid-base equilibrium in the absence of renal insufficiency or vomiting.

The material comprised a group of forty normal infants who were born at the New York Nursery and Child's Hospital and who were made available for this study through the courtesy of the obstetric staff. In all respects these infants were similar to the group concerning which a report was made in the first paper of this series.[1] The ages varied from 1 to 9 days and the birth weights from 2,690 Gm. (5 pounds and 15 ounces) to 4,370 Gm. (9 pounds and 10 ounces), with an average for the group of 3,540 Gm. (7 pounds and 13 ounces). Each infant had been submitted to the routine schedule of feeding of this hospital, which consists of breast-feeding every six hours on the first day, every four hours on the second day and every three hours on the third and subsequent days. In addition, they were offered, and usually took, ½ ounce (15 cc.) of a 5 per cent solution of dextrose after each nursing.

METHODS

The blood was drawn from the anterior jugular vein and carefully protected from air by the use of liquid petrolatum. Venipunctures were always made at the same time of the day and from two and one-half to three hours after the last feeding, so that diurnal variations and those due to digestive processes were eliminated as far as possible.

6. Hasselbalch, K. A.: Ueber die wahre Natur der acidotischen Konstitution des Neugeborenen, Biochem. Ztschr. **80**:251, 1917.

7. Yllpö, A.: Beitrag zur Azidosis bei Neugeborenen. Ueber den Anteil der verschiedenen Blutbestandteile (Hämoglobin, Blutkörperchen, CO_2, Serumsalze) und der Regulation der Blutreaktion, Acta paediat. **3**:235, 1924.

The methods for determining carbon dioxide and chlorides have been given in the first paper of this series.[1] The method for determining p_H was also the same (Hastings and Sendroy's[8] bicolorimetric method), with the exception of the substitution of hundredth-normal hydrochloric acid for the thousandth-normal hydrochloric acid recommended by Hastings and Sendroy for the preparation of the color standard tubes.[9] However, the results obtained in the present series both for new-born infants and for normal adults are notably lower than the figures for p_H given in the first paper. Determinations of p_H made on the serum from six normal adults in conjunction with these investigations gave values ranging from 7.37 to 7.42. The average (7.38) approximates that reported by Cullen and Earle (from 7.4 to 7.5[10]). At present, we can offer no explanations for the differences in p_H reported in this and in the previous paper.

The protein content of the serum was calculated from the refractive index, Neuhausen's formula[11] being used. The base-binding power of protein was calculated by the modification of the Van Slyke formula recommended by Oard and Peters.[12] This formula assumes a constant relation of albumin to globulin of 1:8. Data on the albumin-globulin ratio in infants are not available, although Darrow[12a] stated that any decrease in protein in the serum of premature infants is at the expense of the globulin fraction. If this observation were applicable to new-born infants, it would tend to make the protein percentages calculated from the refractive index on the basis of an albumin-globulin ratio of 1:8 a trifle too high, since the refractive index of globulin is greater than that of albumin. Further work on this subject is in progress at the present time.

The use of the refractive index for determining serum protein also necessitates the assumption that the refractive index of the nonprotein elements of the serum is equal to a constant factor. Consequently, it is possible that the protein values reported in this paper do not represent the actual protein content of the serum, but they may be accepted as a fair estimation and be used for comparative purposes in the absence of more reliable figures. In twenty-one simultaneous determinations of serum protein of older infants and children, made by refractive index and by the Kjeldahl method, the average values were 5.81 per cent and 5.02 per cent, respectively. The average for six normal adults, obtained by the refractive index,

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8. Hastings, A. Baird, and Sendroy, Julius, Jr.: Studies of Acidosis: XX. The Colorimetric Determination of Blood p_H at Body Temperature Without Buffer Standards, J. Biol. Chem. **61**:695, 1924.

9. In some instances the serum was so yellow that the p_H could not be estimated by the colorimetric method. In these cases, a p_H of 7.4 was assumed in calculating the base-binding power of bicarbonate and protein.

10. Earle, I. P., and Cullen, Glenn E.: Studies of the Acid-Base Condition of Blood: I. Normal Variation in p_H and Carbon Dioxide Content of Blood Sera, J. Biol. Chem. **83**:539, 1929.

11. $$\frac{\text{R.I. serum} - \text{R.I. distilled water} - 0.0022}{0.00194} = \%\ \text{protein in serum.}$$ (Neuhausen, B. S., and Rioch, D. M.: J. Biol. Chem. **55**:353, 1923).

12. BP (mM) $= 1.072 \times$ Gm. protein per 100 cc. serum $\times$ ($p_H = 5.04$). (Oard, H. C., and Peters, J. P.: The Concentration of Acid and Base in the Serum in Normal Pregnancy, J. Biol. Chem. **81**:9, 1929).

12a. Darrow, D. C., quoted by Peters, J. C., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, p. 663.

was 7.38 per cent, as compared with an average of 7.01 per cent reported by Salvesen.[13]

The total base content of the serum was determined by the Stadie and Ross[14] method. The preliminary ashing was carried out in pyrex tubes, and the solution was then transferred to platinum dishes. Phosphorus was not precipitated.

TABLE 1.—*Acid-Base Balance of the Serum of Forty Normal New-Born Infants*

Case	Age, Days	p_H of Serum	Carbon Dioxide Content of Serum per Cent by Vol.	Bicarbonate, mM	Carbon Dioxide, Tension, Mm.	Sodium Chloride, Mg. per 100 Cc. Serum	Chloride, mM	Serum Protein		Total Acid Determined, mM	Phosphate, Sulphate and Organic Acid, mM	Total Fixed Base, mM
								Per Cent	mM			
81	9	7.43	50.8	21.7	33.8	...	.....	5.20	13.0	.....	....	149.9
82	5	....	43.1	18.5	29.3	639	109.3	7.28	19.4	147.2	10.3	157.5
83	6	7.40	45.1	19.2	32.1	665	113.7	6.89	17.4	150.3	5.0	155.3
84	8	7.37	50.3	21.3	38.1	633	108.3	6.51	16.3	145.9	4.9	150.8
86	4	7.40	59.3	25.2	42.1	616	105.4	6.48	16.4	147.0	....	143.2
87	7	7.41	53.6	22.8	37.2	616	105.4	6.31	16.0	144.2	8.1	152.3
88	5	7.41	52.9	22.5	36.8	604	103.3	6.29	16.0	141.8	13.1	154.9
89	5	7.40	51.6	21.9	36.7	594	101.6	5.14	13.0	136.5	12.4	148.9
92	7	7.38	50.3	21.4	37.3	597	102.1	5.56	13.9	137.4	10.8	148.2
93	7	7.42	52.0	22.2	35.3	603	103.1	5.79	14.8	140.1	5.0	146.1
94	3	7.42	48.4	20.6	32.9	654	111.8	6.26	16.0	148.4	....	.....
95	4	7.33	42.0	17.7	34.7	651	111.4	7.71	18.9	148.0	2.6	150.6
96	6	7.43	57.0	24.3	37.9	629	107.6	6.46	16.6	148.5	....	141.3
97	7	7.37	50.8	21.5	38.5	622	106.4	6.08	15.2	143.1	7.7	150.8
98	4	7.43	48.9	20.8	32.5	628	107.4	6.41	16.4	144.6	....	144.4
99	6	7.47	56.6	24.2	34.4	637	109.0	6.55	17.2	150.4	3.3	153.7
100	5	7.42	49.6	21.1	33.7	641	109.6	5.77	14.7	145.4	....	.....
101	6	7.38	51.4	21.8	38.1	603	103.2	5.44	13.6	138.6	5.6	144.2
102	6	7.41	55.4	23.6	38.5	631	108.0	5.79	14.7	146.3	17.4	163.7
103	4	7.38	47.5	20.2	35.2	685	117.2	7.51	18.8	156.2	14.6	170.8
104	7	7.44	54.0	23.1	35.1	633	108.3	5.98	15.4	146.8	7.8	154.6
105	1	7.38	53.7	22.8	39.8	617	105.6	5.95	14.9	143.3	3.4	146.7
106	1	7.42	60.7	25.9	41.3	604	103.2	5.85	14.9	144.0	....	.....
107	6	7.38	51.1	21.7	37.9	650	111.3	6.96	17.5	150.5	6.6	157.1
108	7	7.38	53.9	22.9	40.0	649	111.0	5.42	13.6	147.5	6.7	154.2
109	3	7.43	50.7	21.6	33.7	666	114.0	6.20	15.9	151.5	5.9	157.4
110	7	7.42	54.9	23.4	37.3	596	102.0	5.71	14.6	140.0	....	.....
111	6	7.42	62.4	26.6	41.5	647	110.7	5.79	14.8	152.1	9.8	161.9
112	2	7.47	48.7	20.9	29.7	596	102.0	6.11	15.9	138.8	12.7	151.5
113	5	7.42	54.8	23.3	37.3	608	104.0	6.22	15.9	143.2	4.3	147.5
114	7	....	57.0	24.2	40.5	609	104.2	6.18	15.6	144.0	13.2	157.2
115	7	7.41	55.2	23.5	38.4	614	105.0	5.82	14.8	143.3	8.4	151.7
116	6	7.32	50.1	21.1	42.4	626	107.1	7.42	18.1	146.3	15.0	161.3
117	8	7.42	57.0	24.3	38.8	628	107.4	6.17	15.7	147.4	12.1	159.5
118	7	....	57.7	24.5	41.0	601	102.7	6.83	17.3	145.4	10.4	155.8
119	4	7.42	45.3	19.3	30.8	602	103.0	7.25	18.5	140.8	3.9	144.7
120	5	....	50.5	21.5	35.9	636	108.8	6.83	17.3	147.6	6.5	154.1
121	1	7.40	51.2	21.8	36.4	601	102.7	5.91	15.0	139.5	2.9	142.4
122	2	7.27	43.3	18.1	40.8	630	107.8	6.03	14.4	140.3	....	.....
123	6	7.38	53.8	22.8	39.9	625	106.9	5.57	14.0	143.7	6.4	150.1
Average		7.40	52.1	22.1	36.8	625	107.0	6.24	15.8	144.9	7.5	152.4

RESULTS

Table 1 gives the figures for the analysis of the acid and base components of the serum of forty normal breast-fed new-born infants. In order to compare these figures with those for normal adults, we have

13. Salvesen, H. A.: Plasma Proteins in Normal Individuals, Acta med. Scandinav. **65**:152, 1926.

14. Stadie, W. C., and Ross, E. C.: A Micro Method for Determination of Total Base in Blood and Serum and Other Biological Materials, J. Biol. Chem. **65**:735, 1925.

collected a series of the latter from the literature.[15] Table 2 presents the averages for the two groups with their respective probable errors. From this table it may be seen that the serum of new-born infants has a lower bicarbonate and higher chloride content than that of adults, the total base being the same for both groups. The sum of anions, other than chloride and bicarbonate, is also approximately the same. Statistical analysis indicates that the differences in carbon dioxide and chloride between the two groups are significant [16] (table 3).

TABLE 2.—*Average Values for Carbon Dioxide Chlorides and Total Base in New-Born Infants and Adults*

	New-Born Infants			Normal Adults		
	Number of Cases	Mean	Probable Error	Number of Cases	Mean	Probable Error
Bicarbonate (mM)	40	22.145	± 0.214	39	27.608	± 0.252
Chloride (mM)	39	106.962	± 0.691	49	102.978	± 0.178
Total base (mM)	35	152.434	± 0.749	41	153.483	± 0.291
Sum of $BHCO_3$ + BCl		129.107			130.586	
Total base minus sum of $BHCO_3$ + BCl		23.327			22.897	

TABLE 3.—*Differences Between Average Figures for the Serum Content of Carbon Dioxide, Chlorides and Total Base in New-Born Infants and Adults*

	Mean, mM	Difference Between Means	Difference of Probable Errors	Difference / Difference Probable Error
Bicarbonate				
Adults	27.60769	5.46269	0.33053	16.5
New-born infants	22.14500			
Chloride				
Adults	102.97755	3.98399	0.71351	5.6
New-born infants	106.96154			
Total fixed base				
Adults	153.48293	1.04865	0.80363	1.3
New-born infants	152.43428			

15. Oard, H. C., and Peters, J. P.: The Concentration of Acid and Base in the Serum in Normal Pregnancy, J. Biol. Chem. **81**:9, 1929. Peters, J. P.; Bulger, H. A., and Eisenman, A. J.: Total Acid-Base Equilibrium in Health and Disease: VIII. Bicarbonate and Chloride in the Serum of Patients with Heart Failure, J. Clin. Invest. **2**:497, 1926. Peters, J. P.; Bulger, H. A.; Eisenman, A. J., and Lee, C.: Total Acid-Base Equilibrium in Health and Disease: I. The Concentration of Acids and Bases in Normal Plasma, J. Biol. Chem. **67**:141, 1926. Atchley, D. W., and Benedict, E. M.: Serum Electrolyte Studies in Normal and Pathological Conditions: Pneumonia, Renal Edema, Cardiac Edema, Uremic and Diabetic Acidosis, J. Clin. Investigation **9**:265, 1931.

16. When the difference between the means is three or more times the difference of the respective probable errors, it is considered significant. The difference of the probable errors is equal to the square root of the sum of the squares of the probable errors of the two means. Pearl, Raymond: Introduction to Medical Biometry and Statistics, Philadelphia, W. B. Saunders Company, 1923, p. 214.

The employment of different methods prevents a comparison of the protein content of the serum of new-born infants and of adults, although the former would appear to have a lower protein content. Our average figure for the forty new-born infants is 6.24 per cent, as compared with an average of 7.38 per cent obtained on six normal adults by the same method (refractive index). Reiss [17] found that the average figures for infants were approximately 86 per cent of the adult level.

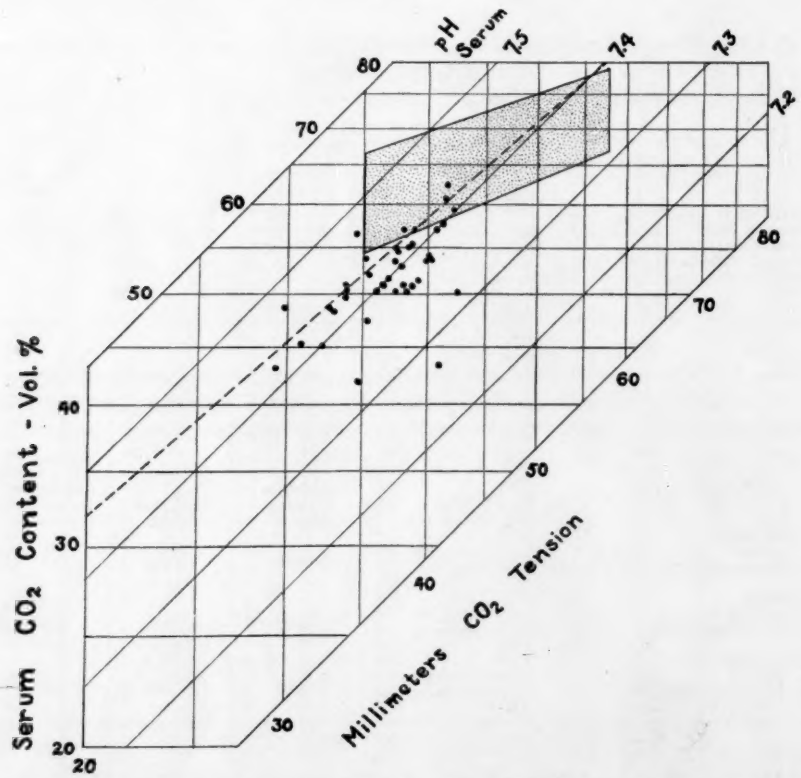

Chart showing the acid-base equilibrium of normal new-born infants plotted on the Peters and Van Slyke logarithmic graph (Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, p. 944). The shaded area represents the normal zone; the dotted line, the division between respiratory and metabolic acidosis.

COMMENT

Mild acidosis is manifested in new-born infants by a decreased carbon dioxide content of the serum. This type of acidosis may arise

17. Reiss, Emil: Die refraktometrische Blutuntersuchung und ihre Ergebnisse für die Physiologie und Pathologie des Menschen, Ergebn. d. inn. Med. u. Kinderh. **10**:531, 1913.

from either of two causes: a primary carbon dioxide deficit or a primary alkali deficit. A chart similar to that devised by Peters and Van Slyke [18] has been constructed in an attempt to ascertain which of these factors plays the predominant rôle in the causation of acidosis in new-born infants (chart 1). From this chart, it is evident that the values for new-born infants that do not lie in the normal range fall in the group of primary alkali deficit with only two exceptions (cases 99 and 112). Eighty-two per cent of the cases fall in the group of alkali deficit and 13 per cent in the normal zone.

Primary alkali deficit may be due to either of two causes: a decrease in the available base in the serum or an accumulation of acid. The average total base for thirty-five infants is practically the same as for adults, so that the first mechanism, characterized by diminution of base,

TABLE 4.—*Daily Variations in the Acid-Base Equilibrium of Normal New-Born Infants During the First Two Weeks of Life* *

	Weight Loss		Carbon Dioxide of Serum		Sodium Chloride of Serum		Serum Protein		Total Fixed Base in Serum	
Age	Ounces	Per Cent of Birth Weight	No. of Cases	Per Cent by Vol.	No. of Cases	Mg. per 100 Cc.	No. of Cases	Per Cent	No. of Cases	mM
Under 24 hours	...	...	9	55.8	7	602	..	....	..	.....
1 day.....	2.8	2.3	7	54.4	7	609	3	5.90	2	144.6
2 days.....	6.0	5.0	10	50.1	9	616	2	6.07	1	151.5
3 days.....	5.8	5.0	8	51.3	6	643	2	6.23	2	149.8
4 days.....	4.6	3.9	12	56.1	12	622	4	7.07	4	150.6
5 days.....	3.7	3.1	16	51.7	14	616	6	6.26	5	154.5
6 days.....	2.4	2.0	18	54.0	17	638	9	6.32	9	154.3
7 days.....	1.5	1.3	19	54.5	18	611	10	5.97	9	152.3
8 days.....	0.6	0.6	9	52.3	9	624	2	6.34	2	155.2
9 days.....	0.1	...	6	53.9	4	636	1	5.20	1	149.9
10-13 days.....	...	...	8	57.2	8	626	..	....	..	.....

* Data for carbon dioxide and sodium chloride reported by Hoag and Kiser (footnote 1) have been included in compiling this table.

may be excluded. On the other hand, the second mechanism is definitely indicated by the high figures for chloride in serum.

Having thus placed the values for new-born infants in the group of primary alkali deficit due to accumulation of chlorides in the blood, the next point for discussion is the origin of this increase in chlorides. Reference to table 4 shows that the chloride content of the blood at birth resembles that of the mother, both approximating the figure for normal adults. Such an accumulation of chlorides as occurs happens after the first twenty-four hours of life and appears to be a gradual increase that reaches its maximum on the third day. This is coincident with the greatest loss of weight. Bakwin [19] has shown that this initial loss of

18. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, p. 944.

19. Bakwin, H.: Dehydration in the New-Born, Am. J. Dis. Child. **24**:497 (Dec.) 1922.

weight is largely due to loss of water, and that the dehydration affects the blood as well as the tissues, as is evident by an increase in the refractive index of the serum. We have also found increases in the serum protein on the second and third days of life coincident with the minimum value for carbon dioxide and the maximum for chloride (table 4). After the third day, these substances show fluctuations, with a gradual trend toward the adult levels. These levels are not reached by the thirteenth day. Further studies in progress at the present time indicate that the chloride returns to normal within the first month of life, but that the low bicarbonate content of the blood persists at least until the second year (tables 3 and 4). The changes observed in new-born infants are all indicative of a mild dehydration that develops rapidly during the first three days of life and then gradually subsides. These alterations in the acid-base equilibrium are parallel but less marked than the changes seen in severe dehydration accompanying gastro-intestinal intoxication.[20]

It has been shown that the high values for chloride in dehydration are largely due to oliguria.[20] Whether or not this is true for infants is still a matter of speculation. New-born infants frequently do not void during the first twenty-four hours of life, and the excretion of urine remains scanty the next day and increases only gradually.[21] This insufficient secretion of urine may lead to a retention in the blood of a portion of the chloride derived from the tissue fluids during this early period of relative dehydration. This explanation would presuppose a normal excretion of base through the stool with a diminished excretion of acid in the urine. The retention of acid would presumably also include phosphate ions, but a retention of phosphorus in the blood cannot be predicted with surety from our data. Phosphorus normally accounts for only 2 mM. of the total acid in the blood, so that even an increase of 100 per cent would have relatively little influence on the acid-base balance of the blood. Until further data concerning the acid output and its concentration in the urine during the first week of life are available, one can only speculate.

The new-born infant passes through a few days of relative starvation immediately after birth. The effect of this starvation, *per se*, might be expected to have some influence on the chemical composition of the blood. Gamble, Ross and Tisdall [22] have shown that in an older child a four-day fast is capable of causing a 25 per cent decrease in the carbon dioxide content of the plasma. At the same time, the total base

20. Hoag, Lynne A., and Marples, E.: Acid-Base Status in Dehydration Accompanying Diarrhea in Infants, Am. J. Dis. Child. **42**:291 (Aug.) 1931.

21. Holt, L. E., and Howland, J.: The Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1926, p. 489.

22. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, J. Biol. Chem. **57**:633, 1923.

remains constant, the difference between total base and acid being made up by ketone acids. Unfortunately, we can present only a very limited number of complete analyses of the blood during this period, so we are unable to state whether or not this is the case in our experiments. However, it would seem that it is not the case; the equilibrium here is being maintained by an increase in the chlorides, a factor introduced, possibly, as a result of water deprivation. The average undetermined acid of fourteen new-born infants, aged 1 to 5 days, was 6.8 mM., which is slightly less than the average of 7.52 for the entire series. This indicates that there is no abnormal increase of ketone acids.

Hyperventilation is another factor the effect of which on the acid-base balance in new-born infants must be considered. Peters, Bulger, Eisenman and Lee [23] reported a decrease in the carbon dioxide content of the blood compensated by an increase in chloride in hyperventilation, both chronic and acute. On the other hand, they found an increase in p_H. The data on new-born infants offer confirmatory evidence for the first two points (reduction in carbon dioxide and increase in chloride) but the normal p_H would tend to preclude hyperventilation as the cause. However, in view of the unreliability of the colorimetric methods for determining p_H, the possibility that hyperventilation may cause at least a part of the reduction of alkali reserve must be kept in mind.

SUMMARY

During the first ten days of life, normal breast-fed infants exhibit a tendency to mild compensated acidosis with a decreased carbon dioxide content of the serum and a normal p_H. This acidosis is of the metabolic type and is due to an accumulation of chloride in the blood. The excess chloride may be due to the lack of sufficient water in the body for the normal excretion of chloride by the kidney. This conclusion must await further data concerning the output and concentration of chloride in the urine during the first week of life. The theory is strengthened, however, by the fact that the most marked alterations in the acid-base equilibrium of the new-born infant occur during the second and third days of life and are coincident with the greatest loss of weight. These alterations parallel, but to a lesser degree, those seen in dehydration accompanying gastro-intestinal intoxication.

161 West Sixty-First Street.

23. Peters, J. P.; Bulger, H. A.; Eisenman, A. J., and Lee, C.: Total Acid-Base Equilibrium of Plasma in Health and Disease: IV. The Effects of Stasis, Exercise, Hyperpnea and Anoxemia; and the Causes of Tetany, J. Biol. Chem. **67**:175, 1926.

SCHICK TEST IN THE NEWLY BORN

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The sensitivity of the skin to intradermal injections of diphtheria toxin in the Schick test is apparently less in the newly born than in older children, although there are certain discrepancies in the results reported. We wish to summarize these briefly and to report the results of a considerable series of tests in newly born infants and their mothers.

The first reported study was made by von Gröer and Kassowitz [1] in Vienna, who found that 23, or 16 per cent, of 143 new-born infants had no demonstrable antitoxin in the cord blood, but only 7 of these (4.9 per cent) gave positive reactions to the Schick test.

Ruh and McClelland,[2] in Cleveland, tested 100 mothers and their new-born infants and found a much higher percentage of positive reactions. Ninety-five mothers and their babies gave corresponding reactions; in 20 instances the reactions were positive in both mother and child, and in 75 they were negative. In 4 instances the mother's reaction was positive while the baby's was negative, and in 1 case a positive reaction was found in the baby with a negative reaction in the mother. In the positive Schick tests in the newly born the authors noted a consistent difference in the intensity of the reaction between the mother and her infant, the mother uniformly giving a more strongly positive reaction than the child.

Kuttner and Ratner,[3] in New York, tested 50 mothers and new-born infants and found that 43 gave corresponding Schick reactions, in 39 cases the test being negative in both and in 4, positive. In the remaining 7 instances the mother's test was positive and the baby's negative or doubtful. They stated that in the 4 infants in whom the

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1. von Gröer, F., and Kassowitz, K.: Studien über die normale Diphtherieimmunität des Menschen. II. Ueber das Verhalten des normalen Diphtherieantitoxins bei Mütter und Neugeborenen, Ztschr. f. Immunitätsforsch. u. exper. Therap. **23**:108, 1915.

2. Ruh, H. O., and McClelland, J. E.: Comparison of Diphtheria Immunity in the Mother and in the New-Born. Am. J. Dis. Child **25**:59 (Jan.) 1923.

3. Kuttner, A., and Ratner, B.: The Importance of Colostrum to the New-Born Infant, Am. J. Dis. Child. **25**:413 (June) 1923.

test was reported as positive the reactions usually reached their height in twenty-four hours, and the test area then faded rapidly so that at the end of forty-eight hours the reaction often appeared negative.

Tests for antitoxin in the blood carried out by the authors cited and by others both on mothers and on their new-born infants have shown that antitoxin is present only in mothers who have negative Schick reactions and in the cord blood of their infants. It is not demonstrable in mothers with positive Schick reactions or in their infants' cord blood.

Because of the differences in the proportion of positive Schick reactions (5, 21 and 8 per cent) obtained in the newly born, a further study of the test in such infants was undertaken. No estimations of antitoxin were made, since it is generally accepted as a result of actual tests that negative Schick reactions in adults occur only in persons with demonstrable antitoxin.

MATERIAL AND METHODS

All mothers and new-born infants were from the wards of the St. Louis Maternity Hospital, and the tests on the infants were made from the first to the tenth day after birth. The mothers varied from 16 to 45 years of age, although almost all were between 18 and 35. Both white and colored women were included, and no selection was made, since the group tested consisted of patients admitted consecutively to the wards.

The toxin employed in the first series, which included 298 cases, was from the New York City Board of Health, while that used in the second series was from one of the commercial laboratories. Both were being used concurrently on other patients and were adequately controlled for their reliability. In every instance control tests with heated toxin were made on both mothers and babies, and the results of every test were read and recorded daily for four days. The skin of young infants is of a somewhat tougher consistency than that of older children and of adults, and intradermal injections are at first slightly difficult on this account. The wheal formed by the injected solution is also slightly smaller.

RESULTS

The preliminary series consisted of 298 mothers and their infants. Ninety-five of these were colored, but since an analysis of the results showed no significant differences between the races, the results for white and colored subjects will be tabulated together. The tests in which the area of reaction measured 20 mm. or more in diameter are marked ++; those in which it was 10 mm. or more but less than 20 mm. are marked +, and those that showed an area of reaction of more than 5 mm. but less than 10 mm. are marked ±. The ± reactions were considered to indicate slight specific skin sensitivity to the toxin, and were not similar to small nodular areas sometimes seen caused by trauma from the needle. They were never noted in control tests with heated toxin. A certain number of mothers gave pseudoreactions and combined

positive reactions, but the heated control tests on the infants were all negative. The positive reactions in infants were almost always of mild intensity, but in 1 infant there was a slight local necrosis on the fourth day. This baby's mother also had a strongly positive reaction.

The results of this first series of 298 tests on mothers and infants are summarized in table 1. It will be noted that 84, or 28 per cent, of the mothers gave positive reactions, while only 51, or 17 per cent, of the infants, had positive Schick tests. Nine mothers and as many infants (3 per cent) gave weakly positive reactions. In a single instance the infant gave a positive reaction and its mother's reaction was negative. The reason for this discrepancy is not clear, although the mother gave the history of having had a positive Schick test and a series of toxin-antitoxin injections three years previously.

Table 1 shows a rather striking relation between the strength of the reaction in the mother and that in her infant. For example, the 48 mothers who gave ++ reactions had only 8 infants (16 per cent)

TABLE 1.—*Comparison of Reactions to Schick Test in Mothers and Infants in 298 Cases (First Series)*

Mother's Reaction	Infant's Reaction				Totals
	++	+	±	−	
++	17	17	6	8	48
+	1	14	3	18	36
±	—	1	—	8	9
−	—	1	—	204	205
Totals.....	18	33	9	238	298

whose reaction was entirely negative, while the 36 mothers whose reactions were + had 18 (50 per cent) babies with negative reactions. Certain other features, especially with regard to the character of the reaction in the babies, will be pointed out in connection with the second series of tests.

Almost a year after the first series of tests was completed, a second group of 345 mothers were tested. The tests were carried out and the measurements recorded as in the first series, and control tests with heated toxin were always included. Seventy-six mothers were colored. In this series, instead of testing the mothers and infants simultaneously, the mothers were given Schick tests first, and only those infants whose mothers gave positive or pseudoreactions were tested. Consequently, only 13 infants of the 236 mothers with negative reactions were tested. It was felt that, from the results of the previous series, all such infants could be assumed to have negative reactions. Because the mother's reaction was read before the Schick test was done on her infant, the

babies were usually tested on from the fifth to the tenth day of life, and in a few instances the child was discharged before the final readings were made on the fourth day.

In table 2 the results of the second series of tests are summarized, the size of the positive reactions being indicated, as previously noted, by + +, + and ±. Of the 345 mothers, 100, or 29 per cent, gave + + or + reactions, and in 9, or 2.6 per cent, the reactions were weakly positive (±); in their infants there were 64, or 18.5 per cent, strongly or moderately positive (+ + or +) reactions and 6, or 1.7 per cent, weakly positive (±) reactions. These figures are almost identical with those for the first series. There is a similar correspondence in the relation between the strength of the mother's reaction and that of her infant, since almost all the infants with positive Schick reactions had mothers with strongly positive (+ +) reactions. Mothers with only moderate (+) reactions and those with weakly positive (±) reactions had a very small number of infants in whom the reaction was positive.

TABLE 2.—*Comparison of Reactions to Schick Test in Mothers and Infants in 345 Cases (Second Series)*

Mother's Reaction	Infant's Reaction				Totals
	++	+	±	−	
++	19	41	6	22	88
+	−	3	0	9	12
±	−	−	−	9	9
−	−	−	−	236*	236
Totals.....	19	44	6	276	345

* Only 13 of these infants were actually tested.

In newly born infants, the type of cutaneous reaction to diphtheria toxin and its course present certain well marked differences from the results in older children and adults. In table 2, there are shown the figures for 100 mothers who gave moderately or strongly positive Schick reactions, while 69 of their babies showed varying degrees of cutaneous sensitivity to the toxin. There is a tendency in many newborn infants for the reaction to disappear earlier than it does in later life, so that if the reading of the infants' tests were limited to the reaction present at the end of the fourth day, which is the usual routine, in many infants that showed definite reactions earlier the test would be called negative. It seems evident that these somewhat modified reactions are due to the specific toxin, since control tests with heated toxin do not produce them.

Because of the variations that occur in the infants' reactions, the size of the individual areas of reaction in the babies of the second series has been shown in table 3. The areas of reaction were always erythe-

matous and well defined. The larger ones were slightly raised and edematous, but in none was there vesication or necrosis. The results tabulated present certain individual differences in size and development of the areas of reaction. While some persist for four days, in the less strongly positive tests they frequently reach their maximum size in forty-eight hours, and many disappear or leave only a brownish staining of the

TABLE 3.—*Schick Reactions in Newly Born Infants Whose Mothers Had Strongly Positive Reactions*

Number		Size of Skin Reaction in Mm.*			
		1 Day	2 Days	3 Days	4 Days
1		7×10	7×10	12×15	..
2		—	10×10	10×12	7×10
3		5× 5	10×12	10×12	10×15
4		5×10	15×20	..	..
5		—	5×10	12×15	10×15
6		2× 2	10×10	..	..
7		7×10	15×20	15×20	..
8		10×15	10×15	15×20	..
9		20×20	20×20	BS	—
10		15×25	15×20	—	—
11		20×25	15×15	15×20	15×25
12		15×20	15×20	15×20	BS
13		10×10	10×15	15×15	..
14		10×15	10×15	10×10	..
15		10×10	10×10	—	—
16		10×15	10×10	—	—
17		10×10	10×10	—	—
18		15×20	BS	—	—
19		15×20	15×20	15×15	..
20		15×15	—	—	..
21		15×20	15×20	—	—
22		10×10	10×15	10×15	10×15
23		10×15	10×15	10×12 (BS)	10×12 (BS)
24		5×10	5×10	..	..
25		15×20	15×20	15×20	..
26		10×15	10×15	—	—
27		10×10	10×10	..	..
28		10×15	—	—	—
29		10×10	10×10	10×10 (BS)	10×10 (BS)
30		10×15	10×15	BS	—
31		15×20	10×15	—	—
32		10×15	10×10	—	—
33		15×20	15×20	15×20	BS
34		10×15	10×15	10×15	10×15
35		15×15	5× 5	—	—
36		5× 7	5×10	10×10	—
37		10×10	5× 5	BS	—
38		20×20	20×25	20×20	10×10
39		20×25	20×25	10×15	10×15
40		5× 5	10×15	15×15	12×15
41		3× 5	8×12	10×15	BS
42		15×20	15×20	15×20	—
43		15×20	15×20	15×20	15×20
44		15×15	10×15	—	—
45		10×12	10×12	7×10	7×10 (BS)
45	Control	7×10	3× 4	—	—

* In this and the following tables, .. indicates no reading made; BS, brownish staining, and —, no visible area of reaction.

skin after the second day. This tendency to more rapid evolution of the reaction than in adults is also seen in some of the more strongly positive reactions. In a few instances the final readings could not be made because the infants had been discharged from the hospital. The last 6 reactions shown in table 3 (nos. 40 to 45) were in infants whose mothers gave strongly positive "combined" reactions. All control tests with heated toxin were negative except one (no. 45), in which the

slight reaction recorded was observed. This was the only instance noted in which a newly born infant showed any evidence of a pseudoreaction.

The reactions shown by the 6 infants (table 2) who had weakly positive (±) Schick tests and the three infants with a moderately positive (+) reaction whose mothers gave only moderately positive (+) reactions are detailed in table 4. The area of hyperemia, while smaller in these babies, was definite, and no reaction whatever was produced by heated toxin. It seems certain, therefore, that these reactions are attributable to specific action of the diphtheria toxin of mild degree. The same tendency to more rapid evolution of the reaction was noted.

The chief differences observed between the cutaneous reaction to diphtheria toxin in infants and that in adults are (1) that certain infants, presumably without antitoxin since they have mothers with positive Schick reactions, give negative reactions; (2) that positive

TABLE 4.—*Weak Positive Schick Reactions Noted in Newly Born Infants*

Mothers' Schick Reaction	Size of Skin Reaction in Mm.			
	1 Day	2 Days	3 Days	4 Days
Strongly positive (++)	2×2	2×3	3×3	5×6
Strongly positive (++)	3×5	5×5	—	—
Strongly positive (++)	5×5	—	—	—
Strongly positive (++)	5×7	—	—	—
Strongly positive (++)	3×5	5×5	—	—
Strongly positive (++)	3×5	—	—	—
Moderately positive (+)	7×10	—	—	—
Moderately positive (+)	7×7	7×10	—	—
Moderately positive (+)	15×15	15×15	10×12	—

reactions in babies tend to develop and to disappear more quickly, and (3) that the cutaneous reactions produced in infants are characterized by a less intense degree of redness and inflammation. Such differences might conceivably be due to a relative decrease in the sensitivity of the skin to the toxin so that larger doses would be required to cause the type of reaction seen in adults, or possibly to some inherent property of the newly born infants' tissues that results in differences in the action of the toxin.

In order to discover the part played by a relative decrease in cutaneous sensitivity to toxin in the new-born, 21 of the infants whose mothers gave positive Schick reactions were given two Schick test doses of toxin as well as the usual test dose (one fiftieth of the minimum lethal dose). Six of these infants gave negative cutaneous reactions to both amounts of toxin, although 4 of their mothers had shown strongly positive (++) Schick reactions and the other mothers moderately positive (+) reactions. The remaining 15 babies gave positive reactions to both doses of toxin, and the results of these tests are shown in table 5. All the mothers of the positively reacting babies had

strongly positive (+ +) reactions. No pseudoreactions occurred in any of the infants, but 4 of the mothers gave combined positive reactions.

In comparing the reactions produced by one and two Schick test doses of toxin in the same infants (table 5), it will be seen that the area of reaction with the large dose of toxin is constantly larger than that produced by the usual Schick test, and the reaction in a few instances remains evident a day longer. Even with the larger amount of toxin, however, there is noted the same tendency for the maximum

TABLE 5.—*Comparison of the Skin Reaction Produced by One and Two Schick Test Doses in Newly Born Infants*

		Size of Skin Reaction in Mm.			
Number	Toxin Dose*	1 Day	2 Days	3 Days	4 Days
1	A	10×15	5×10	5× 5	—
	B	20×25	20×25	15×20	BS
2	A	10×10	10×15	10×15	7×10
	B	10×25	20×25	20×20	20×20
3	A	10×15	10×15	10×15	10×10
	B	20×25	20×25	20×25	20×20
4	A	10×10	BS	—	—
	B	15×15	BS	—	—
5	A	15×20	15×15	15×15 (BS)	—
	B	30×30	25×30	15×15	BS
6	A	5× 5	5×10	5× 5	—
	B	10×10	15×15	15×15	—
7	A	5×10	BS	—	—
	B	10×15	BS	—	—
8	A	5×10	5× 5	—	—
	B	20×20	10×12	—	—
9	A	10×15	10×10	—	—
	B	25×25	15×15	15×15	—
10	A	15×20	15×20	10×10	..
	B	20×30	20×25	15×25	..
11	A	10×10	—	—	—
	B	20×25	20×20	10×10	—
12	A	12×15	10×10	—	—
	B	20×20	20×20	10×10	—
13	A	10×15	10×10	5× 7	—
	B	20×25	20×25	10×10	—
14	A	15×20	15×15	BS	—
	B	20×25	20×25	15×15	—
15	A	20×25	20×20	—	—
	B	30×40	25×30	—	—

* A indicates the skin reaction produced by the usual Schick dose of toxin (1/50 of the minimum lethal dose), and B that produced by twice as much toxin.

reaction to appear before the fourth day and for the reaction to disappear before that time.

These results indicate that the type of cutaneous reactivity to diphtheria toxin is of a different character in the new-born as compared with older persons, and the more rapid development of positive reactions may mean that injury to the tissues shows itself more quickly in early infancy. The early disappearance of the reaction is more difficult to explain but may be evidence of a more limited ability of infants' tissues to react to toxic injury.

SUMMARY AND COMMENT

The results in the two series of Schick tests on mothers and new-born babies were consistent and showed that the majority of babies whose mothers had positive Schick reactions gave positive reactions. Certain mothers with positive Schick reactions, however, had infants who gave negative reactions, even though such babies presumably could have no transmitted antitoxic immunity. Such nonreacting infants were found in relatively small numbers when their mothers gave strongly positive reactions, but those mothers who gave reactions of less intensity had a larger percentage of infants who gave negative reactions. For example, in the group of 643 Schick tests (tables 1 and 2) on mothers and newly born infants, approximately 30 per cent of the mothers and 20 per cent of the infants gave positive reactions. In all the cases in which mothers had positive Schick tests, the infants gave positive reactions in 63 per cent of the tests. However, when the mothers had strongly positive reactions, 78 per cent of their babies gave positive reactions; when the mothers had moderately positive reactions 55 per cent of the babies gave positive reactions and when the mothers' reactions were weakly positive only 9 per cent of the babies had positive reactions.

It is apparent that only a certain number of infants whose mothers have positive Schick reactions fail to react to the toxin, and relatively few (12 per cent) babies whose mothers give strongly positive reactions have negative tests. This direct relation between the degree of the mother's cutaneous sensitivity to the toxin and that of her infant would suggest strongly that the infant's cutaneous reactivity is directly attributable to some transmitted antibody. Variation in degree of reaction in mothers who give positive Schick reactions must be due to variations in antitoxin content in different persons, so that those who give the strongest reactions would be expected to have less antitoxin than those who show weaker positive tests. The antitoxin content of the newly born infant at birth is probably identical with its mother's. It has been shown that those infants who give positive Schick reactions have mothers with the least antitoxin, while in those infants whose mothers have a larger amount of antitoxin, as evidenced by weaker reactions, the reactions tend to be negative. It would seem justifiable to suggest the possibility that less antitoxin is required in newly born infants to prevent the development of a positive Schick reaction than in adults. To demonstrate this would probably require methods for testing the antitoxin content of the blood of greater delicacy than those available at present.

The demonstration of a direct relation between the degree of sensitivity of the mother and that of her new-born infant does not support

the suggestion of others to explain the observation of babies with negative Schick reactions when the mothers give positive reactions, namely, the technical difficulty of the production of intradermal reactions in the new-born and a possible more rapid diffusion of toxin in the infant's skin so that it is not held for a sufficient time to produce a local reaction.

Two differences were shown in the appearance and the development of the reaction to the Schick test in the new-born. The positive reactions were, in general, of a lesser degree of intensity than in adults, and showed only a moderate degree of tissue reaction, even when the area involved was rather large. There was a well marked tendency in many infants, also, for positive reactions to develop more quickly than in adults and to disappear by the fourth day. This may be evidence of a more rapid action of diphtheria toxin on the tissues of newly born infants and may be related to the observation that those who have reported the use of antitoxin in diphtheria in the new-born have found it ineffective.

With relation to the differences in cutaneous reactivity to diphtheria toxin observed in the new-born, the recent work of Wadsworth and Hoppe [4] is worth considering. As a result of experiments with cultures of tissues they found that rapidly growing embryonic cells possess the power of neutralizing or destroying diphtheria toxin. Only when the quantity of toxin exceeds a certain limit is its action injurious. This property is lacking in tissue cells that are not actively growing. The newly born tissues are obviously closely related to embryonic tissue and in active growth, so that they might reasonably be expected to possess a limited ability to neutralize diphtheria toxin that is not present in adult tissue. Such neutralizing power would explain the attenuation of the Schick reactions observed in the new-born.

It is of some interest, in discussing the cutaneous reactivity of newly born infants, to compare the sensitivity to diphtheria toxin shown by the Schick test with that observed for scarlatinal streptococcus filtrate toxin in the Dick test in such young babies. In a group of 200 mothers and their infants studied by one of us (Dr. Cooke [5]), the Dick test was positive in only 1 per cent, while the 53 mothers with positive Dick tests had 2 infants, or less than 4 per cent, who gave a positive reaction. In the group of Schick tests here reported, positive reactions were found in 20 per cent of all the newly born infants and in 63 per

4. Wadsworth, A., and Hoppe, E. N.: The Neutralization or Destruction of Diphtheria Toxin by Tissue, J. Exper. Med. **53**:821 (June) 1931.

5. Cooke, Jean V.: Scarlet Fever. I. The Relation between Antitoxin in the Blood and Skin Sensitivity to Toxin in New-Born Infants and in their Mothers, Am. J. Dis. Child. **34**:969 (Dec.) 1927.

cent of those infants whose mothers had positive Schick reactions. This striking discrepancy emphasizes the fundamental difference in the nature of the sensitivity of the skin to these two toxins, as has been pointed out elsewhere.[6] Diphtheria toxin produces a true toxic injury in tissues not protected by specific antitoxin, while the scarlatinal streptococcus filtrate toxin reacts only when the skin has acquired an allergic sensitivity which, in the new-born, has not yet been acquired.

6. Cooke, Jean V.: The Relation of Bacterial Allergy to Scarlet Fever, J. Allergy **1**:22 (Nov.) 1929; footnote 5.

MECHANISM OF HEMOPHILIA IN INFANCY AND IN CHILDHOOD

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Hemophilia, a clinical chimera for many a bleeding problem, is too rare a condition to cover so many hemorrhagic disturbances, is too hereditary a disease to include so many mature bleeders, is too well defined a disease entity to become a haphazard label of hemorrhagic confusion. A solitary hemorrhage for the first time requires that every local cause be excluded before a diagnosis of hemophilia is ventured. Profuse hemorrhage at birth [1] is varied in origin unless inheritance makes hemophilia a consideration. A prolonged clotting time alone is never pathognomonic of hemophilia. Such common correlations with hemophilia have confused the literature to such an extent that Bulloch and Fildes [2] of the London Eugenic Laboratory have been able to authenticate only 44 hemophilic families of 273 reported in a century of literature.

Hemophilia is of primary concern to the pediatrician, because it first becomes manifest at about the first year of life and continues throughout childhood. Curiously enough, all the trauma incident to birth never precipitates the onset of hemophilic hemorrhage from any part of the new-born infant's body. The dangers from bleeding begin either with artificial trauma incident to development or with sudden surgical intervention. But these dangers wane with the years until early manhood, since the child's body is evidently able to correct the hereditary defect in the course of growth and development. Nevertheless, one half of hemophilic children die before acquiring immunity from this chronic infirmity because of inadequate medical supervision.

In our study of hemorrhagic diseases,[3] my associates and I have been concerned with hemophilia for the formulation of the criteria necessary for diagnosis, for the quantitative determination of the clotting substances involved in blood coagulation, for the determination of the nature of the clotting defect, for the interpretation of the mechanism of hemophilia and finally for the development of a practical mode of

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1. Kugelmass, I. N.: M. Clin. North America **14**:1523, 1931.
2. Bulloch and Fildes: Univ. London Eugenics Lab. Memoirs, 1911, vol. 12.
3. Bancroft, Kugelmass and Stanley-Brown: Ann. Surg. **81**:1, 1929.

management of the hemophilic child. Hemophilia is a well defined disease, and so precludes any possibility of pseudohemophilia. The criteria both necessary and sufficient for the diagnosis of hemophilia may be summarized as follows: (1) hereditary in origin, a family history; (2) limited to males, from infancy to early manhood; (3) tendency to repeated bleeding, spontaneous or traumatic; (4) prolonged clotting time and normal bleeding time, and (5) blood-clotting function deficient and platelets defective.

CRITERIA FOR DIAGNOSIS

Hereditary Nature of Hemophilia.—One of the most remarkable features of the disease is that it runs in families, an observation recorded by the earliest writers on hemophilia. Though the ancients knew of the disease, its first mention was in the eleventh century by Albucasis, the great surgeon of the Moorish period, who described boys who died of uncontrollable bleeding. Classic cases were later described by Benedictus (1539), Hochstetter (1627), Banyer (1743), Fordyce (1781), Consbrush (1793) and Rave (1796). It was not considered a distinct disease entity, however, until 1803, when Dr. John C. Otto,[4] a physician of Philadelphia, published "An account of an Hemorrhagic Disposition Existing in Certain Families." Otto stated that "Males are only affected and all are liable to it." "Though females are free they are capable of transmitting it to their children." Nasse,[5] in 1820, made the first careful study of the pedigrees of hemophilic persons and formulated the universally accepted generalization that males alone are bleeders, the disease being transmitted by apparently normal females through their marriage with normal males.

Subsequent experience led Grandider to state that hemophilia was the most heritable of hereditary diseases. The disease is transmitted to males from generation to generation through the females. It is a recessive sex character linked to a single male chromosome. It may be dormant for many generations only to reappear in some remote male descendant. Its incidence follows the laws of mendelian inheritance. The female conductor transmits the condition to about two thirds of her offspring, and the rest are not conductors. In many families, the ancestral taint has been present for over a century. Each of these families usually has a number of bleeders to characterize the transmission of the disease [6] (table 1).

Mating 1: A hemophilic man will not have children with hemophilia, provided he marries a normal woman. Sons of a hemophilic man are

4. Otto, J. C.: Med. Repository, New York **6**:1, 1803; M. & Phys. J. **20**:69, 1808.

5. Nasse, C. F.: Arch. f. med. Erfahr. **1**:385, 1820.

6. Macklin: Am. J. M. Sc. **175**:218, 1928.

normal and cannot transmit hemophilia. Daughters of such a person will be normal, but all will transmit hemophilia to half their sons.

Mating 2: A woman carrier of hemophilia married to a normal man will transmit the defect to half her daughters and to half her sons as hemophilia. The other children will be normal.

Mating 3: Theoretically, it is possible for a girl to show hemophilia, provided her father was hemophilic and her mother a carrier. This is made impossible of realization, because the presence of a double quantity of the defects acts as a lethal factor inhibiting the development of the embryo.

Normal males of a hemophilic family may marry, but all daughters of hemophilic males are carriers and should not reproduce. Even in a hemophilic family with some normal females, marriage should be prevented, because it is impossible to predict who are carriers and who are free from the defect until they reproduce.

TABLE 1.—*Characteristics of Transmission of Hemophilia* *

	Parents		Offspring	
Mating	Male	Female	Male	Female
1	x hemophilic	XX normal	X normal	Xx carrier
2	X normal	Xx carrier	X normal x hemophilic	XX normal Xx carrier
3	x hemophilic	Xx carrier	X normal x hemophilic	Xx carrier xx hemophilic (?)

* X and x are sex chromosomes. X stands for a normal person, x for a hemophilic carrier. A normal X is dominant to the hemophilic x whose presence is thus concealed when combined with a normal X. The female possesses two sex chromosomes, one inherited from either parent, while the male possesses but one derived from his mother.

Hemophilia Confined to Males.—The immunity of the female sex from hemophilia has been observed since the first published case by Consbrush in 1793. Many have since repudiated this view and have asserted that females may show the less pronounced forms of hemophilia. A pointed argument advanced from analogy to other sex-limited diseases—color blindness and pseudohypertrophic muscular palsy—considered as confined to the male sex is the occurrence of undoubted cases in females. Bulloch and Fildes' critical study of the hemophilic families of the last century revealed no abnormality beyond that which might be observed in any collection of females taken at random. Bucura [7] showed conclusively that all alleged hemophilia among females reported in the literature did not fulfil the necessary and sufficient criteria for the diagnosis of the disease.

7. Bucura: Ueber Hemophili beim Weibe, Vienna, Hölder-Pichler-Tempsky A.-G., 1930.

No convincing evidence has therefore appeared that justifies the diagnosis of hemophilia in the female or the statement that it is transmitted by the male. Immerman's contention that hemophilia in the female awaits some method of diagnosis that does not depend on outward symptoms may be dismissed, for biochemical examination of the blood-clotting components were found normal in mothers of our hemophilic male patients (table 2). The absence of typical hemophilia in the female has been explained by Little and Gibbons,[8] who, on the basis of an analysis of cases filed in the Eugenic Records Bureau, say that a sex-linked lethal factor eliminates the affected females from inclusion among these patients. Kubányi [9] observed that in families with hemophilia, the males whose blood group corresponded to that of the mother were afflicted, while those of a different group escaped hemophilia. Group IV appeared the most prevalent in patients with severe hemophilia.

Hemophilic Tendency to Bleeding.—Physical integrity disturbed by trauma passes unnoticed in a normal child but manifests itself by hemor-

TABLE 2.—*The Concentration of Clotting Components of the Blood of Mothers of Hemophilic Persons*

Case	Date	Pro-thrombin	Fibrino-gen	Anti-thrombin	Platelets	Lysis, per Cent	Index
Mrs. M.	4/12/30	0.84	0.74	1.07	230,000	35	0.5
Mrs. B.	12/ 3/28	1.38	0.84	1.00	400,000	45	1.2
Mrs. G.	4/19/28	1.00	0.75	0.96	210,000	52	0.7
Mrs. C.	8/12/31	1.00	0.64	1.00	165,000	35	0.4

rhage, with no tendency to stop in the usual manner, in a hemophilic child. A significant feature of the disease is not so much the occurrence of bleeding or the rapidity of blood flow, but rather the duration of the bleeding. It persists for hours and often for days and weeks as a slow trickling or oozing away from the surface, in spite of treatment, and may even be exsanguinating. Spontaneous arrest of the bleeding occurs after the patient has been reduced to a state of anemia.

The hemorrhage may be external or internal. The blood may issue from any area of the broken skin or be suffused beneath it, constituting the typical bruise, ecchymosis or hematoma. The blood may also escape into internal cavities or be lost to the body by way of excreta. There is great variation in the ease with which different hemophilic persons may bleed, as well as in the same person at different times, and the severity of the hemorrhage may depend somewhat on the point that has been traumatized. Mucous and serous membranes are relatively low in substances that promote coagulation as compared with the skin.

8. Little and Gibbons: Proc. Soc. Exper. Biol. & Med. **18**:111, 1921.
9. Kubányi, A.: Klin. Wchnschr. **5**:321, 1926.

This accounts for the short bleeding time from a pin prick or a clean incision through the skin in contrast to the profuse bleeding that may follow lacerations of mucous membranes.

Hemophilia becomes manifest by hemorrhage from the nose and gums more commonly than from any other mucous membranes, and particularly by hemorrhage into the joints. Epistaxis is of common occurrence in bleeders, and even if alarming does not alone justify the diagnosis of hemophilia. Hemorrhage from the mouth following the eruption of the milk teeth frequently heralds the onset of the disease. The umbilicus at birth is rarely a site of hemorrhage in hemophilia. The large number of umbilical hemorrhages quoted in the literature as hemophilia are either infections or syphilitic or hemorrhagic disease of the new-born. Articular effusions constitute one of the most typical features of the disease, the knee and elbow joints being most commonly affected. Freund [10] showed that bleeding occurs first in free joint spaces, later in synovial tissues in which hematoma forms and finally in subperiosteum and bone marrow. The accumulated blood remains at a great tension in the joint. And once a hemorrhage has occurred in a joint, the result is a locus minoris resistentiae with chronic susceptibility to recurrence.

Hemophilic bleeding is in the majority of cases definitely traced to trauma. Various attempts have been made to draw a sharp line of demarcation between the two types of hemophilia or even to attribute the spontaneous hemorrhages to small traumas that have escaped attention. In my experience, hemorrhages occurring in the hemophilic child are precipitated either by trauma or by infection. I believe that the so-called type of spontaneous bleeding in hemophilic persons is due to the presence of some intercurrent infection in the body, at least in children. Experimental evidence indicates that the presence of infection markedly disturbs the clotting mechanism in the direction of bleeding in hemophilic persons.

The first manifestations of hemophilia are seen in 70 per cent of the cases before the second year. The trauma incident to birth is not productive of hemorrhage in a hemophilic infant because of the presence of the mother's thrombocytes in the blood of the new-born. It is not until external artificial trauma is induced in the form of ritual circumcision, division of a frenum linguae, piercing of the ears or ragged severance of an ill tied cord that the onset of hemophilia is heralded. Otherwise, the first year of life is usually free from hemophilic warning, but with the beginning of walking hematomas, in connection with other criteria, suggest the hemophilic state. Nevertheless, in the milder cases bleeding first occurs with surgical intervention—extraction of

10. Freund: Virchows Arch. f. path. Anat. **256**:158, 1925.

teeth, tonsillectomy, myringotomy, etc. The liability to hemorrhage is always chronic. There is a progressive decrease, however, in the number and degree of the hemorrhages occurring, so that by maturity the individual is usually free from his infirmity. Schloessmann [11] observed hemophilia to manifest itself as characteristically different in each of the family groups studied. Each of the 24 families with bleeders among the 1,600 members showed definite types of bleeding, sites of origin, intensity and periodicity to be characteristic of each family.

Prolonged Clotting Time of Hemophilic Blood.—The earliest attempts to interpret the nature of hemophilia were to subject the bodies to postmortem examination. Nothing of fundamental importance was revealed by these studies of the vascular system. Pathologists have noted, however, for some time that the shed blood did not clot or did so only imperfectly after an abnormally long interval. But it was not until Wright [12] devised his instrument for measuring the time taken for coagulation that the question was placed on a firmer basis. He noted a constant increase in the clotting time of hemophilic blood as compared with normal blood. Difference of opinion arose. Sahli [13] demonstrated that blood obtained by venipuncture alone, unaltered by tissue products, gives constant values, and even the clotting time is indicative only during the interhemorrhagic period and not during or immediately after a severe hemorrhage.

The bleeding time in hemophilia is normal. This means that the duration of a hemorrhage that follows the puncture of the ear is less than three minutes. This may appear paradoxical, for hemophilia is characterized by bleeding. But a simple pin prick does not cause abnormal bleeding, so that one may safely puncture a vein, finger or ear for purposes of examination. Mucous membranes have a relatively low content of tissue clotting substances, so that slight trauma of the mucosae or joints is often followed by distressing hemorrhage. Fine punctures of the skin make for the development of sufficient tissue clotting substance to coalesce the blood platelets. They form platelet thrombi and thus arrest the bleeding. But scratches usually cover too large a cutaneous area to enable the arrest of bleeding. The distinctiveness of the normal bleeding time in hemophilia, according to Duke, is an established fact, although it does not pertain to the bleeding tendency in active hemophilia.

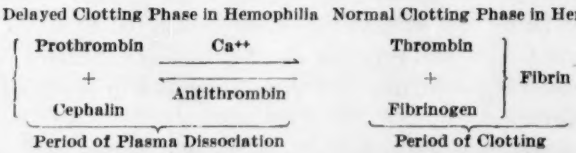
Blood-Clotting Function Deficient in Hemophilia.—Normal blood is endowed with the protective power of resolving itself into a solid felted mass, the clot, effectually sealing up an inflicted wound and thus pre-

11. Schloessmann: Arch. f. klin. Chir. **133**:686, 1924.
12. Wright, A. E.: Brit. M. J. **2**:1306, 1891.
13. Sahli, H.: Ztschr. f. klin. Med. **54**:264, 1904.

venting a fatal issue. This biochemical property whereby a change in the environment of intravascular blood results immediately in a gel constitutes a physiologic function of invaluable service in the maintenance of the physical integrity of the living being. Hemophilic blood differs from normal blood in that it is less sensitive to extravascular changes and gels rather slowly. Hemophilic blood looks like normal blood and is like it in composition, but it functions differently; the basis for its function is independent of all other tissue functions of the body. The mechanism of hemophilia involves an alteration in the blood-clotting function evaluated in terms of the clotting substances contained in blood.

Coagulation of blood is, clinically, the conversion of dissolved fibrinogen by thrombin into insoluble stringy fibrin. This constitutes the clotting phase, which is normal in hemophilia. But the preliminary period during which thrombin is formed is greatly delayed in hemophilia.

The first biochemical study was made by Sahli,[14] who found a decrease in cephalin both in the wounded tissues of the bleeders and in the formed elements of their blood. This observation was confirmed



by Émile Weil,[15] who showed that blood obtained by venipuncture from hemophilic persons remained fluid for several hours, whereas that obtained by finger puncture clotted more rapidly. This rôle of tissue products was further demonstrated by Morawitz,[16] who accelerated the clotting of hemophilic blood by the addition of tissue extracts. Comparative tests with tissue extracts obtained from hemophilic and normal persons have shown, according to Addis [17] and Minot and Lee,[18] that the deficiency is in the formed elements of the blood rather than in the body tissues of hemophilic persons.

Quantitative determinations of the other substances necessary for coagulation of blood have yielded variable results in persons with hemophilia. Klinger [19] found fibrinogen unaltered in quantity and in quality. Wohlisch [20] showed that the thrombin concentration is normal

14. Sahli, H.: Ztschr. f. klin. Med. **56**:264, 1905.
15. Weil, P. E.: Bull. et mém. Soc. méd. d. hôp. de Paris **23**:1001, 1906.
16. Morawitz, P.: Deutsches Arch. f. klin. Med. **94**:110, 1907.
17. Addis, T.: J. Path. & Bact. **15**:425, 1910.
18. Minot, G. R., and Lee, R. I.: Blood Platelets in Hemophilia, Arch. Int. Med. **18**:474 (Oct.) 1916.
19. Klinger, J.: Klin. Med. **85**:335, 1918.
20. Wohlisch, E.: Ztschr. f. d. ges. exper. Med. **36**:3, 1923.

in hemophilic persons. Nolf [21] determined the blood calcium concentration in such persons and found it consistently normal. Repeated findings of normal concentration in the substances actively involved in the clotting mechanism has led to the inevitable conclusion that the defect in hemophilic blood is delay in the conversion of prothrombin into thrombin. All contemporary research has been mainly directed toward elucidating the cause of this delay. Sahli [22] demonstrated that the retarded clotting process was due to deficiency of thrombokinase. Feissly [23] found that the inhibitor substance, antithrombin, prevented formation of thrombin. Howell [24] actually observed inadequacy in prothrombin.

The platelets of hemophilic blood have been found to be more stable than those of normal blood by Howell and Cekada.[25] This slowness of platelet disintegration partly accounts for the delayed clotting in hemophilia. I have observed that the unwashed platelets obtained from hemophilic children were strikingly resistant to disintegration by contact with wet surfaces in comparison with those of normal children. Pickering,[26] however, found that the addition of saponin to hemophilic blood (1: 10,000) completely disintegrates the platelets, but the blood nevertheless remains unclotted for thirty minutes. Blood platelets of hemophilic blood washed with isotonic saline solution disintegrate more rapidly than the unwashed platelets. This indicates that they are protected colloidally by plasma, the difficulty, therefore, being due to a markedly stable blood plasma. We have attempted to correlate these findings in the present studies on blood, so that they may be utilized as additional diagnostic means in hemophilic problems.

Differential Diagnosis of Hemophilia.—The question of hemophilia usually arises in a case of immoderate and uncontrollable hemorrhage or in a case of swelling of a joint. Local causes for every type of hemorrhage, particularly epistaxis, hematoma and hematemesis, must be considered and excluded before hemophilia is considered. These forms of bleeding are so common that it is easy to construct a pedigree showing an inherited hemorrhagic tendency, and reports of such families are extremely common in the literature.

Demonstration of inheritance is essential for the support of the diagnosis of hemophilia, without considering it to have arisen *de novo* in a particular case. The instances of probable hemophilia without demonstrated inheritance are comparatively few and would undoubtedly

21. Nolf, P.: Traité du sang de Gilbert, Paris, 1913.
22. Sahli, H.: Deutsches Arch. f. klin. Med. **99**:518, 1910.
23. Feissly, R.: Schweitz med. Wchnschr. **54**:81, 1924.
24. Howell, W. H.: Arch. Int. Med. **13**:76 (Jan.) 1914.
25. Howell and Cekada: Am. J. Physiol. **76**:500, 1926.
26. Pickering, J. W.: Blood Plasma, London, William Heinemann, Ltd., 1918, p. 210.

be still fewer if physicians had sufficient time, interest or perseverance to investigate beneath what might be immediately apparent on the surface.

It is further essential to establish that the patient has been more or less subject to hemorrhages from various parts of the body. No solitary hemorrhage, however inexplicable, should ever be regarded as a result of hemophilia. It is necessary to show repeated attacks of bleeding from infancy. Diagnosis therefore depends on the family history, the occurrence of repeated and protracted bleeding from several sites, manifestations in the joints and prolonged clotting time of the blood. Mild cases are rare and are not suspected until some accident or operation takes place.

In infants, when as yet there has been no opportunity to observe a chronicity in the disease, diagnosis may be made by the very low index of blood clotting function. Umbilical bleeding, unless present at birth and in the presence of a history of inheritance, should not be considered as hemophilia. In infants within the first week of life hemorrhagic disease of the new-born occurs. It is neither familial nor recurrent, and develops only in the first days of life when the hemophilic infant seldom bleeds. Hemorrhagic disease of the new-born occurs in either sex, but hemophilia never does so.

Hemophilia must be sharply differentiated from chronic purpura hemorrhagica, which occurs in either sex and is neither congenital nor familial. In hemophilia the physiologically defective platelets are present in normal or increased numbers, the bleeding time is normal and the firm clot retracts, but the clotting time is greatly prolonged. In purpura hemorrhagica the number of platelets physiologically normal is much decreased, the bleeding time is prolonged, the clot is nonretractile and soft, and the clotting time is normal. Spontaneous bleeding and purpuric skin lesions are evidence of purpura hemorrhagica and not of hemophilia. Prolonged clotting is not pathognomonic of hemophilia, but occurs also in sepsis, jaundice, polycythemia and nephritis, although not as markedly as in hemophilia. The blood is always found to be normal in scurvy, familial epistaxis, hereditary hemoptysis and hereditary hematuria.

REPORT OF CASES OF HEMOPHILIA

CASE 1.—C. M., a boy aged 2 years, was admitted to the hospital because of hematomas that had developed in the course of play. The skin showed several ecchymotic areas over the extremities. There were some edema and purplish discoloration about the right eye. The blood picture was that of anemia secondary to hemorrhage. The smears showed an increase in reticular cells. The clotting time was fourteen minutes, and the bleeding time three minutes. The child first began to bruise readily at the age of 10 months, but there had been no bleeding

from the mucous membranes. He was born full term, delivery was normal, no instruments were used, and there were no disturbances at birth. There was no family history of hemophilia, other members of the mother's family being unmarried women. The mother's first baby had died at the age of 10 days, following profuse hemorrhage from the umbilicus after minor surgical repair.

CASE 2.—P. G., a white boy aged 7 years, a patient of Dr. Gleich, was admitted to the Harlem Hospital because of continuous bleeding for two days after a fall. All attempts to arrest the bleeding at home by a physician were without avail. On examination, the child showed persistent oozing of blood from the gums without any clot formation. There were small ecchymotic areas over the extremities, but no other hemorrhagic manifestations. The bleeding tendency was first observed in infancy, when, after slight injuries, the child bled from the mucous membranes to such an extent that transfusions of blood were necessitated in neighboring hospitals. There was no history of bleeding in the mother's family. Special dietary regimen showed no favorable effects on the hemophilic state.

CASE 3.—D. M., a boy, aged 10 years, was admitted to the hospital with hemorrhage under the tongue and into both knee joints. The hemorrhagic onset was at 2 years of age, when he began to bruise easily whenever the skin surface was scratched. The present hemophilic arthritis was a recurrence of an illness at 8 years of age. The knees showed massive infiltration of blood, with black and blue spots over the surface. There was considerable limitation of motion. The hemorrhage at the base of the tongue was bordered by a clot, the decomposition of which produced a cadaverous odor. Plaster of paris bandages were applied to both lower extremities to mobilize the knee joints and to protect them from further trauma. A hemophilic history was obtained from the mother's side of the family, a brother having been a bleeder.

CASE 4.—B. S., a young man, was admitted to the hospital for treatment for hemorrhage from lacerations of the right shoulder after falling on cut glass. There was a steady oozing of blood from the wounds even after suturing. Bleeding had begun at the age of 18 months as nosebleeds, and periodically there was observed easy bruising after unsuspected skin trauma. At the fourteenth year, he had a hemorrhagic effusion into the joints, resulting in limitation of motion. At the eighteenth year, he had laceration of the left side of the chest with continuous bleeding, necessitating a transfusion of blood. The epistaxis that initiated the bleeding gradually diminished in occurrence in the course of the patient's growth. There was a family history of bleeding on the mother's side.

CASE 5.—J. H. L., a boy, aged 6 years, was admitted to the hospital, bleeding profusely from a very small wound in the right foot. The bleeding was the result of a scratch made by a piece of glass. A local physician attempted to arrest the bleeding by a compression bandage, but when the mother informed him of previous bleedings, the boy was hospitalized. After loosening useless soft clots, a cut of only 5 mm. in length was observed. Cephalin solution was applied without pressure to avoid trauma and tetanus antitoxin was administered. The blood showed mild anemia secondary to hemorrhage. The smears showed occasional normoblasts and an increase in the reticular cells, evidences of active blood regeneration. At about the second year of life the child had begun to bruise easily, particularly about the ankles. The periodic attacks, the history of bleeding on the mother's side, the prolonged clotting time and the normal bleeding time confirmed the diagnosis of hemophilia.

REPORT OF CASE OF NONHEMOPHILIC BLEEDING

CASE 6.—B. S., a boy, aged 9 years, was admitted to the hospital for tonsillectomy. Three hospitals in the city had advised the procedure, but their surgeons had been unwilling to perform the operation because of the child's history of bleeding since infancy, although the clotting and bleeding times had been found normal preliminary to hospitalization in each case. Hemorrhage first occurred during circumcision, although there were no previous hemorrhagic manifestations for a week after birth. The second hemorrhage in the course of the first year of life followed myringotomy. Since the patient had begun to walk, bruising was observed again and again, and no specific measures taken were effective in obviating further ecchymosis.

This case is illustrative of many misdiagnosed as hemophilia. The boy's index of clotting function was 0.2, which a high protein diet

TABLE 3.—*The Effect of High Protein Diet on the Blood-Clotting Function of Nonhemophilic Bleeders*

Case	Date	Prothrombin	Fibrinogen	Antithrombin	Platelets	Platelet Disintegration, per Cent	Index
B. S.	9/25/28	0.66	0.54	1.57	250,000	24	0.20
	10/23/28	0.81	0.54	1.32	300,000	33	0.30
	11/23/28	0.87	0.54	1.25	205,000	31	0.40
M. H.	9/17/28	0.60	0.60	1.50	175,000	37	0.20
	10/31/28	0.93	0.60	1.07	190.000	31	0.50
J. T.	6/21/29	0.87	0.32	1.07	350,000	30	0.20
		1.06	0.37	1.07	350,000	31	0.30
B. F.	2/19/—	0.66	0.64	1.25	180,000	30	0.35
	3/13/—	0.66	0.64	1.25	220,000	36	0.35
M. M.	4/12/—	0.66	0.37	1.25	150.000	27	0.20
	6/28/—	0.81	0.48	1.07	239,000	30	0.35
D. B.	11/26/28	0.93	0.28	1.25	210,000	52	0.20

elevated to 0.4. A tonsillectomy was then performed without any postoperative bleeding.

Similar cases are given in table 3. The clotting index of B. F. remained the same because of lack of therapeutic cooperation. D. B. was an intern whose bleeding tendency was associated with his strict vegetarian diet. He refused to include protein in his dietary, and suffered from profuse hemorrhage following tonsillectomy. Nonhemophilic bleeders respond readily to high protein, serum and calcium therapy in contrast to persons with hemophilia.

PROCEDURE FOR DETERMINATION OF THE INDEX OF BLOOD CLOTTING FUNCTION

Prothrombin Index.—Blood obtained by cutaneous puncture was drawn into a Wright tube containing 0.1 cc. of 1 per cent sodium oxalate and centrifugated. One-tenth cubic centimeter of the plasma was placed in three tubes (6.8 by 1.3 cm., flat bottom) in a water-bath at 38 C., and to these were added, in series, 0.1, 0.2 and 0.3 of 0.5 per cent calcium chloride. The shortest clotting time in the series was the prothrombin time. The prothrombin index was the ratio of the clotting of the control blood to that of the patient's blood.

Antithrombin Index.—Blood obtained by cutaneous puncture was drawn into a Wright tube, allowed to clot and then centrifugated; 0.1 cc. of serum was drawn off into a small test tube by means of a capillary pipet and heated in a water bath at 60 C. for ten minutes. (Prothrombin was thus destroyed.) Control blood was carried through the same procedure. The heated serums were cooled, and to each was added 0.3 cc. of prepared thrombin solution. The tubes were placed in a water bath at 38 C. The antithrombin index was the ratio of the clotting time of the patient's blood to that of the control.

Fibrinogen Index.—Blood was drawn into a tube containing 0.2 cc. of 3.5 per cent sodium citrate, and was centrifugated under albolene. The refractive index of 1 drop of the plasma at 38 C. was estimated by means of a Pulfrich refractometer. One-tenth cubic centimeter of 15 per cent of calcium chloride solution ($CaCl_2$) was added to the tube to coagulate the fibrinogen, and was then centrifugated. The refractive index of a drop of the serum was then determined. The

TABLE 4.—*Prothrombin Test*

Oxalated Plasma, Cc.	0.5 per Cent Calcium Chloride, Cc.	Clotting Time at 38 C.	
		Control	Patient
0.1	0.1	3 minutes	x
0.1	0.2		
0.1	0.3		

TABLE 5.—*Antithrombin Index*

Heat Serum, Cc.	Thrombin, Cc.	Fibrinogen, Cc.	Clotting Time at 38 C.		Incubation Time
			Control	Patient	
0.1	0.3	0.5	5 minutes	x	15 minutes

percentage of the blood fibrinogen was the difference between the indexes of plasma and serum multiplied by the factor 0.187.

Platelet Count.—Blood was drawn with a red blood count pipet and diluted with 3 per cent citrate (1:200) without the addition of any stain as a diluent. The cell was allowed to stand for ten minutes before the platelets were counted in the customary counting chamber.

Platelet Lysis Index.—Blood was collected into a short tube coated with paraffin, and platelet counts were made at fifteen minute intervals, only those that were single and not agglutinated into clumps being counted. The platelet lysis percentage was the fraction of the platelets that disintegrated within one hour.

Composite value of the ability of blood to clot may be calculated from these determinations. Certain of the blood substances, i. e., prothrombin, fibrinogen and platelets, tend to favor clotting, and others (antithrombin) tend to reverse this process, i. e., favor bleeding. In this chemical mechanism the activity for clotting or bleeding is proportional to the concentration of each active substance.

$$\text{Prothrombin} + \text{Platelets} \rightleftarrows \text{Fibrinogen} + \text{Antithrombin}$$

This reaction expressed in terms of the law of mass action is as follows:

$$\frac{(\text{Prothrombin}) \times (\text{Fibrinogen}) \times (\text{Platelets})}{(\text{Antithrombin})} = 1$$

Introducing normal values for these substances, one has:

Prothrombin 1
Fibrinogen = 0.5 per cent
Platelets = 200,000
Platelet lysis = 50 per cent in 1 hour
Action platelets = 100,000
Antithrombin index = 1

The normal index of the clotting function of the blood is, therefore, 0.5 ± 0.2. Values over 1 indicate a marked tendency to clot, and values below 0.2 indicate a marked tendency to bleed.

The clotting function index has been a more accurate clinical criterion of the condition of the patient than has hitherto been available by laboratory methods. In certain chronic diseases, however, in which the platelets have been markedly increased, no direct relation has been observed between the unusually high clotting index and the possibly increased blood coagulability. We have therefore evaluated the clotting function from the limiting factors:

$$1 = \frac{(\text{Prothrombin}) \times (\text{Fibrinogen})}{\text{Antithrombin}}$$

The normal index thus becomes 0.5 ± 0.2.

RESULTS

The Index of Blood Clotting Function in Hemophilia.—The paucity of actual knowledge about hemophilia led Immerman to come to the conclusion that the standstill is due to the fact that further discussion of the condition is without profit until some method of diagnosis is devised that does not depend on outward symptoms. This my associates and I have found in the development of the methods for the determination of the blood clotting constituents, the data for which are given in table 6 for true hemophilic subjects.

The results show that hemophilic blood has a prothrombin concentration that is less than one third of the normal content. This relatively low prothrombin content is compensated by a correspondingly high antithrombin concentration, which is always more than three times the normal concentration. The platelets of hemophilic blood are always less than 33 per cent in comparison with those of normal blood, which are greater than 50 per cent at the end of an hour from the time blood is obtained from the vein.

The index of clotting function constitutes the ratio of the concentration of the substances tending to clot over those tending to favor bleeding. Hemophilic blood is always characterized by a clotting index that is less than one tenth of the normal, or less than 0.05 in comparison with the normal of 0.5. Any blood the index of which is less than 0.05 may be characterized as hemophilic in a laboratory diagnosis, independent of the other criteria necessary for the diagnosis of

hemophilia. No other hemorrhagic disease with normal platelet count has thus far evinced a blood clotting index as low as that which characterizes hemophilia. The value of resorting to this laboratory procedure for the diagnosis of hemophilia is unparalleled by any other procedure, because it is an absolute criterion for unmistaken diagnosis. We have been able by this means to rule out the presence of hemophilia in females of families that are bleeders or even in mothers of hemophilic boys. We have further been enabled to test the relative merits of therapeutic procedures advanced for hemophilia.

The Differentiation of Hemophilic from Nonhemophilic Subjects by the Index of Blood Clotting Function.—Bleeders of all kinds have come under our observation with the tentative diagnosis of hemophilia. A careful study of each case as indicated in this paper, correlated with the

TABLE 6.—*The Concentration of Clotting Components and the Index of Blood-Clotting Function in Hereditary Hemophilia*

Case	Age, Years	Date	Prothrombin	Fibrinogen	Antithrombin	Platelets	Platelet Disintegration, per Cent	Index
C. M.	2	11/11/30	0.12	0.46	5.7	305,000	30	0.009
C. B.	4	7/ 3/31	0.33	0.64	4.1	370,000	32	0.05
D. B.	6	3/ 5/28	0.13	0.56	6.8	300,000	10	0.003
P. G.	5	5/ 9/30	0.22	0.64	3.6	360,000	34	0.036
D. A.	7	4/19/29	0.22	0.64	5.0	300,000	..	0.02
C. M.	10	8/ 8/30	0.11	1.04	6.5	700,000	37	0.017
J. R.	20	2/13/31	0.11	0.54	6.2	200,000	30	0.01
E. S.	30	9/12/29	0.21	0.54	6.2	230,000	12	0.02
Normal			1.00	0.50	1.0	250,000	50	0.50

determination of the blood-clotting constituents, has reduced the number to the few reported. The other cases (table 3) have been liberated from the dread of the hemophilic label and particularly from the restrictions consequent on the disease. These children have all shown a clotting index well within the normal range, and have responded to nutritional therapy to the extent of alleviating the bleeding tendency, thus enabling them to undergo required operative procedures without hesitation and without needless parental fear.

The Effect of Transfusion in Hemophilia.—Whole blood injected intravenously from a donor of the same group is at present most effective in arresting bleeding. According to the data in table 7, the index of blood clotting function shows a manifold increase following transfusion, but blood determinations made daily have shown that this increase in clotting constituents lasts for only forty-eight hours. Repeated transfusions are necessary for the maintenance of a higher level of clotting function. No change in the clotting index has been observed in hemophilia with manifestations in the joints. Patients with any other type of bleeding occurring in the course of active hemophilia are definitely benefited by transfusion.

The universal protection of the female from the bleeding deficiency that characterizes the male with hemophilia has led several workers to utilize women donors. We have been unable to draw any definite conclusions with regard to this procedure. We have, however, attempted to inject ovarian extract and preparations of the female sex hormone without observing any change in the concentration of the blood-clotting constituents. The daily injection of these substances has not altered the index of blood-clotting function in the least. While we believe that the introduction of blood contributes actual clotting substances to hemophilic blood to accelerate coagulation, it also adds a hormone, sex-linked, which may catalyze the synthesis of clotting compounds. We have

TABLE 7.—*The Effect of Transfusions on the Blood-Clotting Function in Hemophilia*

Case	Date	Prothrombin	Fibrinogen	Antithrombin	Platelets	Platelet Disintegration, per Cent	Index	
E. S.	9/12	0.21	0.54	6.20	230,000	12	0.02	
	9/13	0.50	0.54	2.50	190,000	16	0.11	Transfusion
	9/14	0.40	0.64	3.00	220,000	13	0.08	
	9/16	0.40	0.74	3.00	240,000	20	0.10	Transfusion
	9/17	0.30	0.79	3.70	190,000	16	0.07	
	9/18	0.50	0.89	2.50	190,000	21	0.16	Transfusion
	9/19	0.50	0.94	2.50	205,000	22	0.19	
J. R.	4/ 8	0.20	0.64	3.75	.....	..	0.03	
	4/11	0.20	0.64	3.75	.....	..	0.03	Transfusion
	4/13	0.22	0.64	3.75	.....	..	0.03	
	4/17	0.22	0.64	3.50	.....	..	0.03	
	4/23	0.25	0.54	3.50	.....	..	0.03	Transfusion
	5/ 1	0.25	0.44	3.20	.....	..	0.04	
	5/12	0.29	0.54	3.20	.....	..	0.04	
	5/14	0.29	0.54	3.20	.....	..	0.04	
	5/21	0.25	0.54	3.50	.....	..	0.04	
C. M.	8/ 8	0.11	1.04	6.50	700,000	37	0.017	
	8/11	0.31	1.30	3.50	685,000	37	0.11	Transfusion
	9/ 9	0.16	0.74	5.00	825,000	37	0.024	

adduced proof of a lack of this substance in the blood of hemophilic subjects.

The Sex Hormone in Hemophilia.—The freedom of the female from hemophilia, the presence of both male and female sex hormones in normal males and the striking effect of fresh blood in hemophilia are observations that may possibly be correlated with the disease. An attempt has therefore been made to isolate the female sex hormone from the urine of hemophilic patients during and between attacks. One-half liter of urine was obtained from each subject and acidified with acetic acid. The urine was extracted with chloroform for ten hours in a Freidrich condenser. The chloroform solution was then distilled until the female sex hormone was concentrated to 50 cc. This solution was evaporated to dryness on a steam bath, and the remaining residue finally dissolved in 2 cc. of olive oil.

Young female rats were anesthetized for the removal of the genital tract. Vaginal smears were made daily to confirm the cessation of the

estrual cycles. A week later, 0.2 cc. of the urine extract was injected into each rat for the artificial development of the estrual cycle. Three of four positive results obtained in controls were considered indicative of the presence of female sex hormone in the urine concentrate. We have been unable to identify the presence of the hormone in four hemophilic persons, although controls were positive. Birch[27] had already obtained similar results. We have nevertheless been unable to affect the clotting mechanism in patients with hemophilia by the injection of ovarian extract and theelin.

The Effect of Diet in Hemophilia.—We have in a previous communication[28] presented evidence that the dietary affects the level of blood-clotting function. We observed that the high protein diet

TABLE 8.—*The Effect of High Protein Diet on the Blood-Clotting Function in Hemophilia*

Case	Date	Prothrombin	Fibrinogen	Antithrombin	Index
D. A.	4/19	0.20	0.64	5.0	0.02
	5/19	0.20	0.74	5.0	0.03
J. R.	3/18	0.17	0.64	5.0	0.02
	5/21	0.25	0.54	3.5	0.03
P. G.	5/ 9	0.20	0.64	3.6	0.01
	6/10	0.20	0.64	3.0	0.06
C. M.	8/ 8	0.11	1.00	6.5	0.01
	9/ 9	0.16	0.70	5.0	0.02
D. B.	3/ 8	0.13	0.56	6.8	0.003
	6/ 8	0.12	0.54	6.8	0.003
C. B.	7/ 3	0.33	0.64	4.1	0.05
	7/10	0.36	0.64	4.0	0.05

increases the concentration of clotting substance in potential hemorrhagic disease, less so in frank hemorrhagic disease and not at all in hemophilia (table 8). The protein substances ingested in the daily dietary are utilized by the liver for the synthesis of the substances necessary for the blood coagulation. The innate deficiency in hemophilia is not in the availability of these substances, but rather in the active clotting compounds. This constitutes a deficiency in the primary stage of the clotting mechanism. We have further observed that the conversion of protein substances is not catalyzed by the ingestion of any of the vitamins now known.

TREATMENT FOR HEMOPHILIA

Severe bleeding may be arrested most satisfactorily by transfused blood from a donor of the same blood group. Transfusion serves the dual purpose of replacing lost blood and of increasing the rate of blood

27. Birch, C. L.: J. A. M. A. **96**:244 (July 25) 1931.

28. Kugelmass, I. N.; Bancroft, F. W., and Stanley-Brown, M.: Am. J. Dis. Child. **39**:471 (March) 1930.

coagulation. Whole blood controls the symptoms of hemophilia for a week. The degree of improvement depends on the amount of blood given. Even small amounts (from 15 to 30 cc.) of transfused blood arrest hemophilic hemorrhages. Feissly [29] has shown that the retarded rate of transformation of prothrombin into active thrombin is brought to the normal rate within thirty minutes of the intravenous injection of blood. While the improvement is only temporary, lasting for two or three days, it may be of sufficient duration to permit surgical intervention.

Serum injected into a hemophilic subject is not very effective in controlling hemorrhage. But fresh serum from man, horse or rabbit injected intravenously (15 cc.) or subcutaneously (30 cc.) brings the clotting mechanism to normal within forty-eight hours, and maintains it normal for a week. Weil [30] introduced the injection of fresh serum in the treatment for hemophilia. Nolf observed it to stimulate the formation of thrombocytes. We have found fresh serum poor in prothrombin but rich in thrombin; therefore the relative immediate improvement after intravenous injection. We have found, further, that the injection of all other serums proved ineffective. Sodium citrate injected intravenously or intramuscularly produces a transitory diminution in the clotting time, but this is followed by marked prolongation of the bleeding time, owing to the destruction of platelets by sodium citrate.

Protein sensitization checks mild bleeding, according to Vines.[31] The nonsensitive patient is given 3 cc. of horse serum subcutaneously. After ten days, he will usually be sensitive and should then receive about 0.2 cc. of the same serum intradermally. As the skin reaction becomes positive, the coagulation time of the peripheral blood falls, and, if bleeding is in progress, it will probably stop. The effect may last for weeks. The skin reaction does not desensitize the patient, so that he is constantly ready to react to other intradermal injections of protein given to check further bleeding.

Locally, the most effective coagulant in hemophilic bleeding is fresh human blood soaked in absorbent cotton and applied after removal of useless clots. Diokorides, in the first century A. D., arrested bleeding with fresh bird's blood applied locally. When fresh normal blood is not available, fresh human serum, tissue juice extracts or meat juice applied locally are equally effective. Cephalin checks bleeding when applied locally, but has no effect when given by mouth or by subcutaneous or intramuscular injection. Neither have other coagulants any effect on the bleeding in hemophilia.

29. Feissly, R.: Klin. Wchnschr. **4**:879, 1925.
30. Weil, P. E.: Presse méd. **13**:673, 1905.
31. Vines: J. Path. & Bact. **15**:427, 1910.

At best, the disease is refractory to treatment. Local applications are usually inefficacious in severe bleeding. Transfusion improves the coagulability of the blood only for a few days, and even then it has little or no effect on effusions of blood into the joints. Various attempts have therefore been made recently to maintain a normal clotting mechanism by dietary measures. Though we have developed dietotherapy in hemorrhagic diseases,[32] we have found our "clotting" diets ineffective in hemophilia.

Lopez [33] observed, nevertheless, that hemophilic persons improved on diets rich in vitamins. Bayo [34] recorded the remarkable effect such diet, together with calcium salts, produced on a hemophilic boy. The blood calcium of this patient rose from 5.7 to 11.4 mg. per hundred cubic centimeters. This bleeding problem simulates Wright's hypothetical "hemophilia calcipriva," and contributes nothing to hereditary hemophilia always characterized by a normal blood calcium. Yet on the strength of this, Lopez, a pharmacist of Madrid, patented vitamin tablets supposedly consisting of vitamins A, B, C and D, and calcium phosphate as specific therapy for hemophilia. Nickau [35] described clinical improvement in two hemophilic subjects following the administration of the Spanish vitamin tablets, but the results are not convincing, for more than two hours were required for the blood to coagulate after treatment for six months. We have observed no beneficial results in hemophilia following concentrated vitamin feeding.

The prevention of hemophilia is a problem of eugenics. The course of the disease cannot be fundamentally altered. Every effort should be made to guard the hemophilic child from traumatism. This limitation of bodily motion should be compensated for by daily massage of the extremities. The improved muscle tone thus becomes an effective buffer against vascular injury. The diet should be rich in visceral protein to make available clotting substances for the blood and to maintain optimum blood regeneration in case of hemorrhage. The child's blood group should be determined, and a suitable donor kept available for emergency transfusion. In case of hemorrhage, the child should be put to bed at absolute rest and given morphine or its derivatives, if necessary. Tissue juice extracts should be applied locally, and transfusion given when the loss of blood becomes marked. This is to be repeated on the third day to arrest hemorrhage and to induce healing more rapidly. The hemophilic child may undergo surgical operation without hemorrhage, provided a large transfusion of blood is previously given.

32. Kugelmass, I. N., and Samuel, E. L.: Am. J. Dis. Child. **41**:48 (July) 1931.
33. Lopez, F. L.: Arch. de med., cir. y espec. **26**:405, 1927.
34. Bayo, P.: Ars med. Barcelona **3**:378, 1927.
35. Nickau, B.: Klin. Wchnschr. **7**:590, 1928.

CONCLUSIONS

1. The criteria necessary and sufficient for the diagnosis of hemophilia have been formulated on the basis of experimental and clinical studies.

2. Quantitative determinations of the constituents involved in blood coagulation show the hemophilic deficiency to be in the primary stage of the blood-clotting mechanism.

3. Hemophilic blood shows a strikingly low prothrombin content compensated by a correspondingly high antithrombin content. The platelets are normal in number but are physiologically defective, having a slow rate of disintegration.

4. Hemophilic blood is characterized by a blood-clotting index that is less than one tenth of the normal. The index constitutes the ratio of the concentration of the substances tending to clot over those tending to favor bleeding. Accordingly, the normal index of clotting function is 0.5, whereas the hemophilic clotting index is less than 0.05. This very low index of blood-clotting function is diagnostic of hemophilia.

5. The index of blood-clotting function shows a manifold increase after transfusion, but the improved clotting lasts for only forty-eight hours. Transfusion does not alter the clotting function of blood in hemophilic subjects with manifestations in the joints.

6. Dietary protein, lipids, vitamins or minerals do not alter the deficient clotting function in hemophilia.

7. Hemophilic persons show the absence of the female sex hormone in their tissues normally present in males. Ovarian therapy, theelin and other products of the female generative organs injected into the hemophilic subject produce no change in the clotting mechanism evaluated quantitatively.

8. Serum injected or applied locally is not effective in controlling hemorrhage in hemophilia, unless it is fresh and rich in thrombin. But nonhemophilic bleeders respond readily to any serum and to dietary protein therapy.

BASAL METABOLISM OF TWENTY-ONE CHINESE CHILDREN REARED OR BORN AND REARED IN THE UNITED STATES*

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During recent years much interest has been centered on the study of racial influence on basal metabolism. Several investigators have reported that the basal metabolism of oriental peoples was lower than that of the occidental races. Others have demonstrated that, irrespective of race, all those who resided in a tropical climate showed a reduced production of heat.

REVIEW OF THE LITERATURE

Table 1 gives a brief summary of a number of basal metabolism values for oriental subjects reported in the literature. Most of them have already been discussed in the recent reviews of Wang and Hawks [1] and of Du Bois.[2] With the exception of the reports of Takahira [3] and that of Okado and his associates,[4] all the values were lower than occidental standards. The former used a modification of the Du Bois height-weight formula for surface area in the calculation of his results and compared the figures thus obtained with modifications for Japanese

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*The experimental work was conducted at the Nelson Morris Memorial Institute for Medical Research of Michael Reese Hospital in conjunction with the dietary study of these children which will be submitted by Jean E. Hawks in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the department of home economics, University of Chicago.

1. Wang, C. C., and Hawks, J. E.: Recent Advancement in the Study of Basal Metabolism in Health and Disease, J. Am. Dietet. A. **5**:87 (Sept.) 1929.

2. Du Bois, E. F.: Recent Advances in the Study of Basal Metabolism, J. Nutrition **3**:217 (Sept.) 1930.

3. Takahira, H.: The Basal Metabolism of Normal Japanese Men and Women, in Progress of Scientific Nutrition in Japan, edited by T. Saiki, Geneva, League of Nations, 1926, publication no. 3, p. 11. Takahira, H.; Kitagawa, W.; Ishibashi, E., and Kayano, S.: The Basal Metabolism of Common Laborers, in Progress of Scientific Nutrition in Japan, ibid., p. 37.

4. Okado, S.; Sakurai, E., and Kameda, T.: The Basal Metabolism of the Japanese, Arch. Int. Med. **38**:590 (Nov.) 1926.

of the Harris-Benedict, Aub-Du Bois and Dreyer standards. The actual number of calories per twenty-four hours obtained by him was as low or lower than the averages given by other investigators. The differences were, however, in most cases, within 10 per cent.

The three studies [5] conducted on Filipinos gave an average of about 5 per cent below the occidental standards. In an extensive study of the basal metabolism of the Chinese, Earle [6] demonstrated that the average results obtained from one hundred and sixty-six Chinese were 8 per cent below the Du Bois standards, and those from five Chinese in London from 6.5 to 8.5 per cent below. His values for thirty-one Chinese in Peiping were only 2.3 per cent lower than the standards, while those for a group of ten non-Chinese orientals in Hongkong gave an average of 10 per cent below, and the heat production of forty-seven westerners living in Hongkong and Peiping was about 7 per cent lower than the occidental standards. The results were also below Benedict and Dreyer's standards.

The three studies [7] conducted on oriental students in the United States gave values even lower than those reported by the authors mentioned. They ranged from 10.2 to 13.8 per cent below Du Bois' standards and from 10.1 to 12.2 per cent lower than Benedict's values. The average figure obtained in Yasutake's study [8] conducted on nine healthy Japanese young men was 34.1 calories per square meter per hour. Although he did not compare his results with any occidental standards, nor did he give the ages of the subjects, it is obvious that his average value is much lower than any of the occidental standards. In a study conducted on fifty-four men and fifty-three women of miscellaneous occupation, Takeya,[9] using also a modification of the Du Bois height-weight formula for calculating the surface area, found that the average value of heat production of men was 37.90 and that

5. Fleming, W. D.: Respiratory Metabolism and Blood Chemistry of Filipinos, J. Metab. Research **4**:105 (July-Aug.) 1923. Sison, A. B. M., and Ignacio, M.: Observations on Basal Metabolism Among Filipinos, J. Philippine Islands M. A. **1**:416 (Nov.) 1927. Ocampo, M.; Cordero, N., and Concepcion, I.: The Basal Metabolism of the Filipinos, ibid. **10**:357 (Sept.) 1930; J. Nutrition **3**:237 (Nov.) 1930.

6. Earle, H. G.: Basal Metabolism of Chinese and Westerners, Chinese J. Physiol. (rep. ser.) no. 1, p. 59, July, 1928.

7. (*a*) Blunt, K., and Dye, M.: Basal Metabolism of Normal Women, J. Biol. Chem. **47**:69 (June) 1921. (*b*) MacLeod, G.; Crofts, E., and Benedict, F. G.: The Basal Metabolism of Some Orientals, Am. J. Physiol. **73**:449 (July) 1925. (*c*) Necheles, H.: Basal Metabolism in Orientals, ibid. **91**:661 (Jan.) 1930.

8. Yasutake, M.: Ueber den Grundumsatz des japanischen erwachenen Mannes, Fukuoka-Ikwadaigaku-Zasshi **17**:58, 1924.

9. Takeya, K.: Estimation of Surface Area and Basal Metabolism of Japanese, Fukuoka-Ikwadaigaku-Zasshi **22**:51 (June) 1929.

of women was 34.86 calories per square meter per hour. He, too, did not compare his results with American standards. His figures are higher than Yasutake's, but there is little doubt that they are still slightly below American standards.

In summarizing, it may be said that all the work reported in the literature was conducted on oriental adults, that the majority of the results gave a basal metabolism value lower than occidental standards, and that no work has been done on oriental people born in occidental countries. In view of these facts, it was deemed interesting to conduct a study on Chinese children born and reared in the United States.

EXPERIMENTAL METHOD

Twenty-one Chinese children, eleven boys and ten girls, between the ages of 5 and 17 served as subjects. With the exception of the 17 year old girl (M) none of the children had reached the age of puberty. All of them were of Chinese parentage, and, excepting three (P. A., H. A. and M.) who were born in China, they were all born and reared in Chicago. In spite of the fact that their parents had been residents of the United States for a long time, their habit of living was little different from that of their ancestors in China. All the children were below the height and weight of American children of average size. All the boys but two and 50 per cent of the girls were slightly underweight, according to the Baldwin-Wood tables, with weight referred to height and ages. Their heights referred to weight and age were well up to the standards of Baldwin-Wood, with an average percentage deviation of +2.5 for boys and +1.1 for girls. The average percentage deviation from standards of weight was —5 for boys and —1.8 for girls. As the children were attending both Chinese and American schools at nearly all hours during six days a week, the metabolism tests were conducted on three or four consecutive Sunday mornings. The children were trained to become accustomed to the test before any experiment included in this paper was conducted. All the metabolism tests were made in the morning when the subjects were in a postabsorptive state after a rest period of not less than thirty minutes. The subjects were kept as nearly as possible under basal conditions, both mental and physical, during the experimental periods. A Tissot gasometer in connection with the Haldane gas analysis apparatus was employed for measuring the heat production, and the average of the two lowest values was used as the basal metabolism of each child.

RESULTS

The results obtained were expressed in terms of total calories per twenty-four hours, calories per kilogram of body weight per twenty-four hours, calories per centimeter of body height per twenty-four hours and calories per square meter of body surface per hour. These values were compared with various American standards.

The total calories per twenty-four hours, as shown in table 2, in the majority of cases varied with age, ranging from 844 to 1,280 for the boys and from 818 to 1,284 for the girls. With the exception of the 17 year old girl (M), whose basal metabolism was markedly low,

TABLE 1.—*Summary of Basal Metabolism Studies on Orientals*

Author	Date	Subjects: Race	Subjects: Occupation	Subjects: Sex	Subjects: Average Age	Subjects: Number	Basal Heat Production: Calories per 24 Hours	Basal Heat Production: Calories per Square Meter per Hour	Percentage Deviation from Standards: Harris-Benedict	Percentage Deviation from Standards: Aub-Du Bois	Percentage Deviation from Standards: Dreyer	Percentage Deviation from Standards: Boothby Sandiford	Percentage Deviation from Standards: Palmer, Means and Gamble	Comment
Fleming	1923	Filipino	Hospital normals	M	22	8	1,356	.....	.....	.....	.....	—5.3	.....	
Sison and Ignacio	1927	Filipino	Hospital	M	11-50	43	.....	35.8 to 41.2	.....	—1.6 to —14.4	.....	.....	.....	Did not include low values in average
			Normals	F	16-60	38	.....	33.2 to 39.4	.....	+6.4 to —13.5	.....	.....	.....	
Ocampo, Cordero and Concepcion	1930	Filipino	Students	M	23	88	1,376	36.8	—5.6	—7.8	.....	.....	.....	
			Nurses	F	22	16	1,146	33.6	—10.6	—9.3	.....	.....	.....	
Takahira	1926	Japanese	Miscellaneous	M	31	73	1,373	37.3	.....	.....	.....	.....	—1.8	
				F	30	43	1,073	33.8	.....	.....	.....	.....	—1.5	
Takahira	1926	Japanese	Laborers	M	33	30	1,475	40.2	+7.6	+8.1	+9.0	.....	.....	Standards similar but not same as American's
				F	38	20	1,174	36.4	+7.3	+11.3	+11.4	.....	.....	
Okado, Sakurai and Kameda	1926	Japanese	Students	M	24	24	1,426	38.7	+0.2	—2.0	.....	.....	.....	
			Nurses	F	21	11	1,258	36.7	—3.9	—0.8	.....	.....	.....	
Earle	1928	Chinese	Miscellaneous	M	21-25	166	1,366 to 1,439	36.8 to 38.7	—2.0 to —9.3	±0.0 to —8.0	—2.0 to —10.0	.....	.....	
				F	21-33	166	1,078 to 1,164	34.3 to 35.0	—6.0 to —11.7	—4.3 to —13.5	—12.0	.....	.....	
Blunt and Dye	1921	Chinese	Student in America	F	21	1	1,239	31.9	—12.2	—13.8	.....	.....	.....	
MacLeod, Crofts and Benedict	1925	Chinese	Students in America	F	21-29	7	1,147	....	—10.4	—10.2	.....	.....	.....	
		Japanese		F	..	2								
Necheles	1930	Oriental	Students in America	M	19-36	8	.....	....	—10.1	—12.3	.....	.....	.....	
Yasutake, etc.	1924	Japanese	Miscellaneous	M	..	9	1,342	34.1	.....	.....	.....	.....	.....	
Takeya	1929	Japanese	Miscellaneous	M	..	54	1,455	37.9	.....	.....	.....	.....	.....	
				F	..	53	1,248	34.9	.....	.....	.....	.....	.....	

all the values were high as compared with the Benedict-Talbot [10] standards. The minimum average percentage deviation from the standards referred to age was + 6.8 for boys and + 11.5 for girls. When our results were compared with the standards referred to weight, the average percentage deviation was + 16.6 for boys and + 18.5 for girls. The corresponding figures referred to height were + 10.5 and + 20.2, and those referred to surface area were + 13.6 and + 19.8. In every instance the deviation was greater in girls than in boys. When the results were compared with Dreyer's [11] standards, the heat pro-

TABLE 2.—*Basal Heat Production per Twenty-Four Hours*

Name	Age	Pulse	Respiratory Quotient	O_2 Consumed per Min., Cc.	CO_2 Produced per Min., Cc.	Average Observed Value, Calories	Percentage Deviation from Benedict-Talbot Standards: Referred to Age	Referred to Weight	Referred to Height	Referred to Surface Area	Percentage Deviation from Dreyer Standard
Boys											
E. C.	5	81	0.835	121	101	844	+ 8.9	+26.7	+13.6	+10.4	— 7.6
H. I.	5	81	0.828	122	101	846	+ 9.1	+11.1	+ 3.9	+ 5.9	—16.7
He. I.	7	82	0.785	133	104	914	+ 1.5	+13.1	+ 7.7	+10.7	—10.9
W. F.	8	77	0.808	148	120	1,028	+ 8.2	+25.8	+16.7	+23.4	+ 1.2
G. E.	9	60	0.798	148	118	1,021	+ 3.1	+21.5	+12.9	+19.0	— 0.3
Sh. C.	9	62	0.854	143	122	997	— 1.5	+13.5	+ 9.5	+13.7	— 5.8
S. D.	9	70	0.814	149	121	1,035	+ 3.1	+10.0	+ 3.1	+ 9.5	— 7.4
V. F.	10	69	0.800	185	145	1,280	+19.6	+23.4	+12.8	+22.1	+ 8.0
H. T.	10	70	0.819	176	144	1,220	+14.0	+12.8	+18.7	+13.5	— 0.5
St. C.	11	61	0.834	172	144	1,200	+ 6.7	+ 8.8	+ 6.0	+ 9.2	— 2.4
F. E.	11	71	0.811	168	136	1,149	+ 2.5	+11.5	+10.5	+12.1	— 1.4
Average.....		72	0.817	151	124	1,049	+ 6.8	+16.6	+10.5	+13.6	— 4.0
Girls											
M. Y.	5	96	0.798	133	106	920	+23.4	+28.9	+32.5	+29.0	+ 1.0
P. A.	6	84	0.826	118	97	818	+ 3.6	+18.8	+24.5	+22.1	— 4.4
H. A.	7	101	0.773	139	107	952	+14.0	+31.5	+34.8	+31.9	+ 7.9
J. E.	7	80	0.804	146	117	1,009	+20.9	+32.4	+33.7	+34.5	+ 9.6
E. L.	9	68	0.795	153	122	1,056	+15.0	+19.7	+15.3	+20.1	+ 4.7
G. M.	9	75	0.813	146	119	1,004	+11.2	+21.6	+13.4	+20.5	+ 6.2
L. F.	12	67	0.885	182	161	1,284	+21.7	+11.0	+12.8	+14.1	+ 8.6
T. C.	13	78	0.842	146	120	1,014	— 7.8	+ 2.4	+ 2.2	+ 4.8	— 3.2
J. T.	14	69	0.796	168	134	1,162	+ 1.5	+ 0.2	+12.6	+ 1.5	+ 0.1
M.*	17	64	0.805	171	138	1,184	+18.8	— 3.2	— 8.6	.....	—10.2
Average.....		80	0.815	148	120	1,024	+11.5	+18.5	+20.2	+19.8	+ 3.4

* Not included in the average.

duction of the majority of the children was within normal limits. The average percentage deviation from his standards was — 4.0 for the boys and + 3.4 for the girls.

When the values of the basal heat production were calculated on the basis of body weight, they varied inversely with age, ranging from 40.7 to 63.9 calories per kilogram of body weight per twenty-four hours for the boys, and from 33.6 to 57.3 calories for the girls, as shown in table

10. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, publ. 302, Carnegie Inst., Washington, 1921.

11. Dreyer, G.: The Normal Basal Metabolism in Man and Its Relation to the Size of the Body and Age, Expressed in Simple Formulae, Lancet **2**:289 (Aug. 7) 1920.

3. The average heat production of the boys was 49.2 calories per kilogram per twenty-four hours, and that of the girls was 47.3 calories. These figures were much higher than the Benedict-Talbot standards referred to weight, with an average percentage deviation of + 16.2 for the boys and + 18.4 for the girls. The corresponding values referred to age were + 25.0 and + 26.2.

Table 4 shows the basal heat production calculated on the basis of height. The values ranged from 7.93 to 9.51, with an average of 8.69 calories per centimeter per twenty-four hours, for the boys. The

TABLE 3.—*Basal Heat Production per Kilogram per Twenty-Four Hours*

Name	Age	Observed Weight in Kilograms	Percentage Deviation from Baldwin-Wood Standards: Weight Referred to Height and Age	Observed Calories per Kilogram	Percentage Deviation from Benedict-Talbot Standards	
					Referred to Weight	Referred to Age
Boys						
E. C.	5	13.2	— 7.8	63.9	+26.5	+38.9
H. I.	5	16.3	— 5.8	51.9	+11.1	+12.8
He. I.	7	18.2	— 4.2	50.2	+13.1	+21.0
W. F.	8	18.5	— 8.4	55.6	+25.8	+39.0
G. E.	9	19.4	— 8.5	52.6	+21.4	+37.0
Sh. C.	9	20.7	— 3.3	48.2	+13.7	+25.5
S. D.	9	23.1	— 9.4	44.8	+10.1	+16.7
V. F.	10	26.7	—13.0	47.8	+22.9	+28.5
H. T.	10	28.6	+ 9.6	42.7	+12.9	+14.8
F. E.	11	26.5	— 0.4	43.4	+11.6	+22.9
St. C.	11	29.5	— 3.6	40.7	+ 8.8	+18.1
Average			— 5.0	49.2	+16.2	+25.0
Girls						
M. Y.	5	16.2	+ 1.3	56.8	+28.8	+35.6
P. A.	6	15.0	+ 2.0	54.5	+18.7	+35.6
H. A.	7	16.6	+ 1.8	57.3	+31.4	+48.1
J. E.	7	18.1	+ 0.6	55.7	+32.3	+43.9
G. M.	9	29.8	— 8.4	48.3	+21.7	+30.5
E. L.	9	23.2	— 4.1	45.5	+19.7	+23.0
L. F.	12	34.4	— 9.4	37.3	+11.0	+ 8.7
T. C.	13	27.6	— 7.1	36.7	+ 2.2	+ 8.9
J. T.	14	34.6	— 7.0	33.6	± 0.0	+ 1.8
M.*	17	47.0	+ 4.2	25.2	— 3.1	.....
Average			— 1.8	47.3	+18.4	+26.2

* Not included in the average.

corresponding values for the girls were 7.64, 9.29 and 8.6. In general, they were more uniform than the values calculated on the basis of either weight or surface area. Thus, the coefficient of dispersion based on weight was 0.1 for the boys and 0.17 for the girls. The corresponding values calculated on the basis of surface area were 0.06 and 0.10, while the coefficient of dispersion with reference to height was 0.04 for the boys and 0.05 for the girls, which shows that a greater uniformity was obtained from the values calculated on the basis of height, and that the values for boys were more uniform than those of girls.

The values for basal heat production calculated on the basis of surface area are listed in table 5. They varied from 45.6 to 59.6

TABLE 4.—*Basal Heat Production per Centimeter Compared with Standards*

Name	Age in Years	Observed Height in Centimeters	Percentage Deviation from Baldwin-Wood Standards: Height Referred to Weight and Age	Observed Calories per Centimeter	Percentage Deviation from Benedict-Talbot Standards
Boys					
E. C.	5	94.6	+5.1	8.92	+13.6
H. I.	5	106.7	+3.6	7.93	+ 3.9
He. I.	7	111.8	+2.6	8.17	+ 7.5
W. F.	8	115.6	+5.6	8.90	+16.7
G. E.	9	117.6	+2.2	8.68	+12.9
Sh. C.	9	118.1	+1.2	8.44	+ 9.5
S. D.	9	127.0	+4.3	8.15	+ 2.0
V. F.	10	137.5	+6.0	9.31	+12.7
H. T.	10	128.3	—4.3	9.51	+18.7
F. E.	11	129.5	+0.1	8.88	+10.6
St. C.	11	137.2	+1.2	8.74	+ 5.9
Average			+2.5	8.69	+10.4
Girls					
M. Y.	5	102.2	—0.8	9.00	+32.5
P. A.	6	97.8	—1.2	8.36	+24.4
H. A.	7	103.5	—1.1	9.20	+34.9
J. E.	7	108.6	—0.1	9.29	+33.7
G. M.	9	121.9	+5.3	8.24	+13.7
E. L.	9	125.1	+1.7	8.44	+15.3
L. F.	12	146.7	+3.8	8.76	+12.6
T. C.	13	132.7	+4.5	7.64	+ 2.1
J. T.	14	136.5	—2.5	8.51	+12.6
M.*	17	145.4	—3.7	8.14	+ 5.1
Average			+1.1	8.60	+20.2

* Not included in the average.

TABLE 5.—*Basal Heat Production per Square Meter Compared with Standards*

Name	Age	Observed Square Meters of Body Surface	Observed Calories per Square Meter per Hour	Percentage Deviation from Benedict-Talbot Standards			Percentage Deviation from Bailey Standard
				Referred to Square Meter	Referred to Age	Referred to Weight	
Boys							
E. C.	5	0.591	59.6	+24.4	+30.7	+27.1	+ 8.4
H. I.	5	0.719	49.0	+ 9.4	+ 7.5	+ 7.2	—1.09
He. I.	7	0.774	49.2	+11.8	+11.8	+10.6	— 7.2
W. F.	8	0.782	54.8	+25.1	+26.6	+23.4	+ 5.4
G. E.	9	0.808	52.9	+22.2	+23.9	+20.5	+ 3.7
Sh. C.	9	0.843	49.2	+14.4	+15.2	+12.8	— 3.5
S. D.	9	0.907	47.6	+11.7	+11.5	+ 8.7	— 6.7
V. F.	10	1.038	51.9	+24.6	+26.3	+23.6	+ 3.8
H. T.	10	1.074	47.3	+15.6	+12.4	+13.4	— 5.4
F. E.	11	1.012	46.9	+12.5	+13.0	+11.7	— 4.3
St. C.	11	1.097	45.6	+12.3	+ 9.9	+ 9.9	— 6.9
Average			50.4	+16.7	+16.9	+15.4	— 2.1
Girls							
M. Y.	5	0.690	55.5	+30.0	+33.7	+33.4	+ 6.7
P. A.	6	0.653	52.0	+20.1	+26.8	+22.9	+ 2.0
H. A.	7	0.702	56.5	+32.9	+38.1	+36.5	+13.0
J. E.	7	0.745	56.6	+35.7	+38.4	+38.4	+13.2
G. M.	9	0.840	50.2	+24.3	+22.7	+25.8	+ 4.6
E. L.	9	0.903	48.7	+21.4	+20.2	+23.0	+ 1.5
L. F.	12	1.173	45.6	+18.4	+13.7	+17.8	+ 1.3
T. C.	13	1.014	41.7	+ 6.4	+ 4.3	+ 6.1	— 5.2
J. T.	14	1.178	41.1	+ 7.0	+ 3.0	+ 6.2	— 4.4
M.*	17	1.446	34.1	.....	—15.4	.....	—14.8
Average			49.8	+21.8	+22.3	+23.4	+ 3.6

* Not included in the average.

calories per square meter per hour for the boys and from 41.1 to 56.6 calories for the girls. The average for the boys was 50.4, and that for the girls was 49.8. In comparison with the Benedict-Talbot standards the values for boys were from 7.2 to 27.1 per cent higher than theirs and those for girls were from 3 to 38.7 per cent higher. The average percentage deviation from the standards for boys was + 16.7, referred to surface area, + 16.9 referred to age and + 15.4 referred to weight. The corresponding values for girls were + 21.8, + 22.3 and + 23.4. Our results were surprisingly close to Bailey's [12] standards. With the exception of the figures for the 17 year old girl and three others, all values were within normal limits. The average percentage deviation for the boys was —2.1, and that for the girls was +3.6.

TABLE 6.—*A Comparison of Basal Heat Production in Chinese-American Children and in American Children of Approximately the Same Range of Age and Degree of Nutrition*

	Chinese-American		American		Deviation	
Children	Range	Average	Range	Average	Calories	Percentage
	Calories per Kilogram per 24 Hours					
Boys	40.7-63.9	49.2	50.0-60.0	52.7	—3.5	—6.64
Girls	33.6-57.3	47.3	35.0-56.0	48.8	—1.5	—3.07
	Calories per Centimeter per 24 Hours					
Boys	7.93-9.51	8.69	8.13-9.28	8.74	—0.05	—0.57
Girls	7.64-9.29	8.60	7.13-9.11	8.31	+0.29	+3.49
	Calories per Square Meter per Hour					
Boys	45.6-59.6	50.4	43.8-59.3	51.7	—1.3	—2.51
Girls	41.1-56.6	49.8	42.1-63.1	51.8	—2.0	—3.86

Perhaps the most interesting comparison is that which was made between the results of the present investigation and those [13] obtained in a group of American children of approximately the same range of age and degree of undernutrition. These children were studied in our laboratory along with our undernourished children, in 1926, and were classified as "normal in weight, but not vigorous." On recalculation of some of the values it was noted that the results for the two groups of children agreed very closely. Regardless of the basis on which comparison was made, the Chinese-American children showed a basal metabolism within normal limits of that for American children. The average percentage deviation, as shown in table 6, was from + 3.49

12. Bailey, C. V.: Calories per Square Meter of Body Surface per Hour, quoted by Hawk and Bergeim: Practical Physiological Chemistry, ed. 9, Philadelphia, P. Blakiston's Son & Co., 1927, p. 896.

13. Wang, C. C.; Kern, R.; Frank, M., and Hays, B. B.: Metabolism of Undernourished Children: II. Basal Metabolism, Am. J. Dis. Child. **32**:350 (Sept.) 1926.

to —6.64. When the values were expressed on the basis of weight, the average basal heat production of the Chinese boys was 6.64 per cent lower than that of the American boys, while that of the Chinese girls was 3.07 per cent below that of the American girls. The corresponding values based on height were —0.59 and +3.49 per cent, and those based on surface area were —2.51 and —3.86 per cent. Thus, in the majority of cases the Chinese children showed a slightly lower basal metabolism than the American children, although the difference is not significant.

COMMENT

The results of the present investigation failed to demonstrate a definitely low basal heat production in American-born Chinese children such as was reported in oriental adults by various investigators. In comparison with the data obtained from oriental adults that were reported in the literature as well as with the Benedict-Talbot standards,[10] our values were surprisingly high. In the majority of cases they were more than 10 per cent higher than the standards. In two hundred and twenty comparisons the negative sign was used only three times. The closest correlation in nine possible comparisons with the standards was that when the results were compared with the values of total calories per twenty-four hours referred to age. The greatest deviation from the standards occurred in the comparison with the values based on weight referred to age. In contrast to the foregoing comparisons our results agreed very closely with both Dreyer's [11] and Bailey's [12] standards. Furthermore, the results of the present investigation agreed remarkably well with the values of one of the groups of children studied in our laboratory in 1926.[13] This close agreement might be due to one or more of the following factors: 1. The age and the degree of malnutrition of the two groups of children were very similar. Both groups were slightly underweight referred to height and age. 2. The families of both groups lived in a poor district in Chicago for many years. 3. Although the apparatus employed for measuring the heat production was different (in our early work Benedict's cot chamber was used, while in the present investigation a Tissot gasometer was employed), the general technic was practically the same in the two investigations. Thus, for instance, the metabolism experiments were conducted when the children were strictly quiet, but wide awake. In contrast to what Necheles [7e] observed in his adult Oriental subjects these Chinese-American children were no more calm or relaxed than American children, as judged by their appearance. Although some Chinese customs were retained in their homes, the children had imbibed American ideas to a great extent. Their diet was undoubtedly still similar to that of their ancestors in China, but in comparison with the Chinese diets described in the litera-

ture, these children consumed less cereal products and more animal proteins. Could it be possible that the slight increase of animal proteins, particularly in the form of meat, might have tended to stimulate their metabolic processes? Or would it be more likely that the climatic conditions were responsible for the higher heat production of the Chinese-American children? With reference to the first theory, although some authors are still in favor of it, many others have questioned its validity. Thus, Asher and Honda,[14] Truszkowski,[15] Hicks,[16] Lieb,[17] Borgstrom and his associates[18] and McClellan[19] have demonstrated clearly that a prolonged high protein diet has little influence on basal metabolism. Their results were substantiated by the findings of Wang and her associates.[20] In regard to the theory of the influence of climate, aside from the numerous reports on the low basal metabolic rate of people of various races living in tropical lands, Sundstroem[21] and Benedict and MacLeod[22] demonstrated that rats in artificially produced tropical climate also had a low basal metabolism. The fact that this might be one of the possible theories was also indicated in Earle's investigation.[6] His results showed that the basal heat production of his Chinese subjects in Peiping was only 2.5 per cent below the standard, while that of the natives of Hongkong was 10 per cent below. Furthermore, westerners in Hongkong had a lower metabolism (7 per cent below standards) than the native

14. Asher, L., and Honda, T.: Action of Meat on Respiratory Metabolism of Rats Fed on Fat, Biochem. Ztschr. **185**:173 (May) 1927.

15. Truszkowski, R.: Studies in Purine Metabolism. III. Basal Metabolism and Purine Content, Biochem. J. **21**:1040 (Aug.) 1927.

16. Hicks, C. S.: Basal Metabolism of Man on Diet Rich in Nucleic Acid, Australian J. Exper. Biol. & M. Sc. **4**:151 (Sept.) 1927.

17. Lieb, C. W.: The Effects of Exclusive Long Continued Meat Diet: Based on History, Experience and Clinical Survey of Vilhjalmur Stefansson, Arctic Explorer, J. A. M. A. **87**:25 (July 3) 1926; Effects on Human Beings of Twelve Months Exclusive Meat Diet: Based on Intensive Clinical and Laboratory Studies on Two Arctic Explorers Living under Average Conditions in New York Climate, ibid. **93**:20 (July 6) 1929.

18. Borgstrom, P.; Hafkesbring, R., and Bost, R. W.: Protein Intake as Indicated by Urinary Nitrogen, Am. J. Physiol. **79**:245 (Dec.) 1926.

19. McClellan, W. S.: Der Einfluss einer einjarhigen aus schliesslichen Fleischkost bei zwei Menschen, Klin. Wchnschr. **9**:931 (May 17) 1930.

20. Wang, C. C.; Hawks, J. E.; Huddlestun, B.; Wood, A. A., and Smith, E. A.: The Influence of High and Low Protein Diet on the Basal Metabolism and the Chemistry of Blood and Urine in Normal Women, J. Nutrition **3**:79 (July) 1930.

21. Sundstroem, E. S.: Some Observations on the Interrelation between Functional Levels of the Animal Body and the External Cooling Power, J. Biol. Chem. **63**:XLI (Feb.) 1925.

22. Benedict, F. G., and MacLeod, G.: The Heat Production of the Albino Rat: II. Influence of Environmental Temperature, Age, and Sex; Comparison with the Basal Metabolism of Man, J. Nutrition **1**:367 (May) 1929.

subjects in Peiping, which shows that climatic conditions may have had a greater influence on the energy metabolism than racial difference. Some of the other possible explanations for the discrepancy between our findings and those reported in the literature are: 1. It is possible that the standards for adults are slightly too high, as was pointed out by Benedict [23] and Du Bois.[2] It may also be probable that the Benedict-Talbot standards for children are somewhat too low, for reasons mentioned in our earlier communications.[24] It has been unfortunate that with the exception of Earle, who made observations on occidental subjects along with the orientals, none of the investigators used westerners as controls. However, studies made on normal controls in various laboratories in this country have generally demonstrated a slightly lowered energy metabolism as compared with the Du Bois and Harris-Benedict standards. 2. It has generally been known that adults relax more easily than children, and it is also possible, as Necheles [7c] pointed out, that oriental adults relax even more easily than do occidental adults. On the other hand, there is apparently little or no difference in this respect in children of the two races. The latter theory is substantiated further by the results obtained from the 17 year old girl (M). In contrast to the high values of all the younger children, her basal metabolism was consistently low. In nine comparisons only twice were her values above the standards. One of the high results was obtained when her total twenty-four hour heat production was compared with the value calculated by Benedict's formula for the prediction of basal heat production per twenty-four hours for women. In this case her metabolism was + 18.8 per cent. When the comparison was made on the basis of calories per centimeter, her metabolism was + 5.1 per cent. The other seven comparisons ranged from — 3.1 to — 15.4 per cent. These values are in agreement with those reported by Blunt and Dye [7a] and MacLeod, Crofts and Benedict.[7b]

In conclusion, according to the present investigation the racial influence plays an insignificant rôle in the metabolism of American-born Chinese children. On account of the small number of children studied, the results should not be considered conclusive. They have, nevertheless, opened an interesting field for further investigation.

SUMMARY

1. The basal heat production of twenty-one Chinese-American children, eleven boys and ten girls, between the ages of 5 and 17 years, was

23. Benedict, F. G.: Basal Metabolism Data on Normal Men and Women (Series II), Am. J. Physiol. **85**:607 (July) 1928.

24. Wang, C. C., and Kern, R.: The Influence of Sleep on Basal Metabolism of Children, Am. J. Dis. Child. **36**:83 (July) 1928. Wang and others (footnote 13).

studied. With the exception of three, all the children were born and reared in Chicago.

2. With the exception of the 17 year old girl (M), all the children had a total heat production above the Benedict-Talbot standards, with an average percentage deviation ranging from +6.8 to +16.6 for the boys and from +11.5 to +20.2 for the girls. In comparison with the Dreyer standards, all the values were within normal limits.

3. When the basal metabolism was expressed in terms of calories per kilogram per twenty-four hours, a greater percentage deviation, averaging between + 16.2 and + 26.2, from the Benedict-Talbot standard was found.

4. When the calculations were made on the basis of height, the values expressed as calories per centimeter per twenty-four hours were much more uniform than those based on either weight or surface area, the coefficient of dispersion being 0.04 for the boys and 0.05 for the girls. The corresponding values based on weight were 0.10 and 0.17, while those based on surface area were 0.06 and 0.10.

5. The average percentage deviation from the Benedict-Talbot standards was from + 16.7 to + 23.4 when the basal heat production was calculated on the basis of surface area. However, the results were surprisingly close to the Bailey standards, with an average percentage deviation of — 2.1 for the boys and + 3.6 for the girls.

6. The results of this investigation were closely comparable to the findings in the group of American children classified as "normal in weight but not vigorous" who were studied in our laboratory in connection with our problem on undernourished children. The present study has, therefore, failed to demonstrate a definite low basal metabolism in Chinese-American children such as several investigators found in oriental adults.

7. Some of the possible causes of the discrepancy between the present findings and those reported in the literature are: (1) the difference in climatic conditions; (2) the difference in standards in adults and in children and (3) the difference in the ability to relax in adults, especially oriental adults, and children.

8. The basal metabolism of the 17 year old girl (M) was lower than the standards. The results in her case were in agreement with those reported in the literature.

IRON IN THE LIVER AND IN THE SPLEEN AFTER DESTRUCTION OF BLOOD AND TRANSFUSIONS

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While making a microscopic study in the pigments of liver, I was impressed with the frequency of hemosiderosis of the liver in young infants as contrasted with its rarity in the liver of adults. Accordingly, I made a microscopic study of the liver and spleen in 100 recent cases that came to autopsy at the Babies' Hospital.[1] The presence of iron in the liver and spleen was determined and the amount estimated by staining with an acidified solution of potassium ferrocyanide for from twenty to thirty minutes.[2] The presence of iron is indicated by its combination with the ferrocyanide to form prussian blue. The clinical facts with regard to hemoglobin, red blood cells, transfusions of blood, etc., were obtained from the histories and were tabulated. From a study of these tables several significant correlations became apparent. In the instances in which transfusions had been given during life (30 cases), iron was microchemically demonstrable in both spleen and liver. In the remaining 70 cases (table 1), iron was found in the spleen and liver in almost all patients under the age of 3 months; in patients over that age it was found rarely in the spleen and very rarely in the liver.

In the liver, iron was seen in the Kupffer and hepatic cells, and when present in fairly large amounts, in the bile canaliculi. In the spleen, iron was seen in the pulp and sinuses, occasionally lying free between the cells, but usually within the phagocytes. The amounts of iron microscopically demonstrable were recorded as follows:

0	None seen	Normal
∓	Occasional blue granule	
±	Small isolated amounts	
+	Moderate amount	Abnormal
++	Abundant amount	
+++	Very abundant amount	
++++	Extremely abundant	

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1. This material was made available for study through the courtesy of Dr. Martha Wollstein.

2. Mallory and Wright: Pathological Technique, ed. 8, Philadelphia, W. B Saunders Company, 1924, p. 207.

TABLE 1.—*Iron in the Spleen and Liver of Young Infants, Tabulated in Order of Age*

Autopsy Number	Age	Sex	Race	Diagnosis	Autopsy Date	Blood			Hemosiderosis		Comment
						Date	Hemoglobin	Red Blood Cells	Spleen	Liver	
5846	1 da.	F	W	Prematurity, intraventricular hemorrhage	6/21/30	.....	...	.....	++	++	6 months' gestation
5919	2 da.	M	W	Hematoma of scalp, hemoperitoneum, icterus neonatorum	12/19/30	.....	...	.....	+	+	Iron in Kupffer cells
5853	7 da.	M	W	Prematurity, meningeal hemorrhages, otitis media (bilateral)	7/ 5/30	.....	...	.....	+	+	6½ months' gestation
5852	7 da.	M	W	Congenital atresia of esophagus, prematurity, meningeal hemorrhage	7/ 3/30	7/ 2/30	150	5,784,000	++	++	Iron present in both Kupffer and hepatic cells
5851	7 da.	F	W	Prematurity, meningeal hemorrhage	7/ 3/30	.....	136	6,088,000	+	+	Twin of patient 5854
5820	7 da.	M	N	General icterus, bronchopneumonia	5/ 7/30	5/ 6/30	125	5,296,000	+	+	
5854	9 da.	M	W	Prematurity, meningeal hemorrhage	7/ 6/30	6/26/30	158	5,808,000	+	∓	Twin of patient 5851; very little iron in liver
5855	15 da.	M	W	Spina bifida, pyomyelia, pyocephalus	7/ 9/30	7/ 3/30	160	5,696,000	+++	++	Liver pigment almost entirely in Kupffer cells
5833	17 da.	M	W	Bronchopneumonia	5/28/30	5/24/30	105	4,104,000	+++	+	
5929	3 wk.	M	N	Bronchopneumonia, fibrinopurulent pleurisy, acute glomerulonephritis	1/24/31	1/22/31	90	4,768,000	++	++	In liver, almost all the iron present in the epithelial cells; very little in Kupffer cells
5910	22 da.	F	W	Congenital peritoneal band, constriction of colon	11/27/30	11/19/30	119	5,500,000	++	++	In liver, most of the pigment lay in Kupffer cells; a small amount in liver cells; 11/20/30, icteric index 55
5816	1 mo.	M	W	Pulmonary edema, fatty liver	4/28/30	4/25/30	87	3,120,000	+++	++	Iron more abundant in liver cells than in Kupffer cells
5935	1 mo.	F	N	Intestinal intoxication, subacute pancreatitis	2/13/31	.....	130	5,690,000	+++	+	In liver, iron present in both Kupffer and hepatic cells
5832	1 mo., 3 da.	F	W	Prematurity, patent foramen ovale and ductus arteriosus	5/26/30	5/10/30	150	5,680,000	++	+	
5835	5 wk.	M	W	Hemorrhage into cerebral ventricle, icterus	6/ 2/30	.....	...	.....	+++	+++	Van den Bergh biphasic ++++; iron abundant in both Kupffer and hepatic cells
5857	5 wk.	M	W	Congenital malformation of heart, bronchopneumonia	7/12/30	6/26/30	98	4,576,000	∓	∓	Very little iron in both organs
5875	5 wk.	M	W	Bronchopneumonia, fatty liver	8/21/30	.....	...	.....	++	++	Iron present in both Kupffer and hepatic cells
5831	1 mo. and 11 da.	F	W	Prematurity, icterus, emphysema of lungs	5/26/30	5/17/30	106	4,480,000	++++	+++	Iron abundant in both Kupffer and hepatic cells
5814	7 wk.	F	W	Meningeal hemorrhage, pulmonary congestion	4/25/30	4/24/30	80	3,392,000	+++	+++	Much iron in both Kupffer and hepatic cells
5898	2 mo.	M	W	Septicemia, Streptococcus hemolyticus, edema of lungs	10/10/30	8/ 6/30 9/26/30	125 60	6,288,000	++	+	In liver, iron present in both Kupffer and hepatic cells

5000	2 mo.	M	W	Bronchopneumonia, edema of lungs	10/15/30	10/14/30	65	3,800,000	++	+	In liver, iron present in both Kupffer and hepatic cells
5873	2 mo.	F	W	Intestinal intoxication, bronchopneumonia	8/18/30	8/11/30	95	4,170,000	++	++	In liver, iron occurred in both Kupffer and hepatic cells
5847	2½ mo.	M	W	Bronchopneumonia, strictures of ureters, hydronephrosis (bilateral)	6/23/30	5/23/30 6/18/30	60 75	2,992,000 1,248,000	++	++	Iron preparation given by mouth; iron present in both Kupffer and hepatic cells
5804	3 mo.	M	W	Prematurity (7 mo.), acute fibrinous pleurisy, acute bronchopneumonia	4/ 8/30	2/28/30	60	3,256,000	+	0	Viosterol given
5827	3 mo.	M	W	Status thymicolymphaticus, operation: repair of cleft palate	5/20/30	.....	...	.....	0	0	
5915	3 mo.	F	W	Congenital cardiac hypertrophy, patent foramen ovale	12/ 6/30	.....	...	.....	0	0	
5897	3½ mo.	M	W	Status thymicolymphaticus, repair of harelip, aspiration of blood into larynx, trachea and bronchi	10/ 9/30	10/ 6/30	70	3,010,000	±	+	In liver, iron present in both Kupffer and hepatic cells
5934	3½ mo.	M	W	Congenital malformation of heart, atelectasis of right lung	2/10/31	2/ 5/31	130	6,460,000	0	0	
5842	3 mo., 21 da.	M	W	Neurogenic contraction of sigmoid, intestinal obstruction, interstitial pneumonia	6/16/30	5/ 1/30	105	6,300,000	+++	+	
5819	4 mo.	F	N	Congenital syphilis, bronchopneumonia, fatty liver	5/ 6/30	4/ 3/30	50	3,580,000	0	0	
5941	4 mo.	M	W	Congenital malformation of brain, internal hydrocephalus	6/16/30	6/13/30	88	4,320,000	+	0	
5802	6 mo.	M	W	Bronchopneumonia, congenital syphilis	4/ 7/30	3/28/30	50	4,416,000	±	±	Viosterol given
5913	6 mo.	M	N	Bronchopneumonia, congenital syphilis	12/ 3/30	11/29/30	?	6,130,000	0	0	Viosterol given
5932	7 mo.	F	W	Bronchopneumonia	2/ 6/31	1/29/31	78	4,944,000	+	0	Viosterol given
5926	8 mo.	M	W	Bronchopneumonia, fatty liver	1/19/31	1/17/31	92	4,668,000	+	0	
5803	8 mo.	M	W	Serofibrinous pleurisy, pericarditis (streptococcus), bronchopneumonia	4/ 7/30	.....	...	.....	0	0	
5918	10 mo.	M	W	Peritonitis (Streptococcus hemolyticus), edema of lungs	12/19/30	.....	...	.....	0	0	
5806	1 yr.	M	W	Purulent pericarditis, fatty liver	4/11/30	.....	...	.....	?	0	
5862	13 mo.	F	N	Intestinal intoxication	7/21/30	10/20/29	59	3,768,000	0	0	
5834	15 mo.	M	N	Bronchopneumonia, acute interstitial nephritis	6/ 2/30	5/14/30	55	4,560,000	+	0	Viosterol given
5930	16 mo.	F	W	Bronchopneumonia, meningitis, (B. influenzae)	2/ 5/31	1/29/31	65	3,760,000	0	0	Viosterol given
5870	16 mo.	F	W	Miliary tuberculosis	8/ 9/30	8/ 1/30	98	5,216,000	0	0	
5801	17 mo.	M	N	Bronchopneumonia, fatty degeneration of kidneys	4/ 6/30	.....	...	.....	0	0	
5860	18 mo.	M	N	Bronchopneumonia, acute otitis media	7/18/30	7/14/30	63	3,792,000	0	0	
5805	18 mo.	F	N	Bronchopneumonia, pulmonary tuberculosis, miliary tuberculosis	4/10/30	4/ 3/30	55	4,480,000	±	0	
5809	18 mo.	F	W	Lobar pneumonia, pulmonary edema, acute nephritis	4/12/30	4/ 7/30	54	3,736,000	±	0	
5843	19 mo.	F	W	Meningitis (B. influenzae), bronchopneumonia	6/18/30	6/13/30	65	5,080,000	+	0	

TABLE 1.—*Iron in the Spleen and Liver of Young Infants, Tabulated in Order of Age—Continued*

Autopsy Number	Age	Sex	Race	Diagnosis	Autopsy Date	Blood			Hemosiderosis		Comment
						Date	Hemoglobin	Red Blood Cells	Spleen	Liver	
5924	19 mo.	F	W	Congenital cardiac hypertrophy, congenital absence of spleen, edema of lungs	1/16/31	6/ 9/30	120	6,016,000	Abs.	0	
5872	20 mo.	M	W	Miliary tuberculosis, tuberculosis of lung	8/10/30	8/ 5/30	65	4,500,000	0	0	
5906	21 mo.	F	W	Lobar pneumonia, suppurative mediastinitis	11/17/30	11/15/30	78	.....	+	0	
5863	21 mo.	F	W	Status lymphaticus, operation (removal of nevus)	7/26/30	.....	60	5,408,000	0	0	
5821	2 yr.	F	W	Tuberculous lymphadenitis, acute miliary tuberculosis	5/ 7/30	5/ 3/30	55	3,550,000	?	0	Spleen not examined
5938	2 yr.	M	W	Meningitis (B. influenzae), bronchopneumonia	3/ 7/31	2/27/31	64	4,064,000	±	0	
5901	2 yr.	M	W	Acute polioencephalitis, focal necrosis in liver	10/22/30	10/21/30	105	5,440,000	0	0	
5845	28 mo.	F	W	Status lymphaticus, removal of cataracts	6/18/30	6/13/30	79	3,656,000	0	0	
5895	2½ yr.	M	N	Tuberculosis of lung, biliary cirrhosis of liver, sickle cell anemia	10/ 4/30	7/16/29 10/ 1/30	51 30	6,024,000 2,310,000	+	0	
5931	31 mo.	F	W	Extensive burn, edema of lungs	2/ 6/31	.....	...	.....	0	0	
5837	33 mo.	M	Chin.	Sarcoma of kidney, fatty liver	6/ 5/30	.....	...	.....	0	0	
5868	3 yr.	F	W	Tuberculous pneumonia, miliary tuberculosis	7/30/30	7/25/30	51	2,848,000	++	0	Albuminized iron given
5874	3 yr.	F	W	Appendical abscess, peritonitis	8/19/30	.....	...	.....	+++	+	In liver, iron present in Kupffer cells; patient died 4 hours after admission
5922	4 yr.	M	W	Lipoid nephrosis, peritonitis (pneumococcus type III)	12/27/30	12/12/30	76	3,360,000	0	0	
5928	4 yr.	M	W	Bronchopneumonia, suppurative pleurisy	1/23/31	1/20/31	71	4,712,000	0	0	
5902	4½ yr.	M	N	Rheumatic pancarditis, tuberculous adenitis	10/27/30	7/ 7/30 10/22/30	80 52	5,360,000 4,064,000	0	0	
5908	4½ yr.	M	W	Tuberculosis of lung, miliary tuberculosis	11/24/30	11/17/30	75	3,550,000	+	0	
5916	5 yr.	M	N	Tuberculous pneumonia, miliary tuberculosis	12/ 8/30	11/25/30	90	5,470,000	0	0	
5818	5 yr., 9 mo.	M	N	Verrucous endocarditis, cardiac hypertrophy, pulmonary edema	5/ 2/30	3/26/30	75	4,370,000	0	0	
5921	6 yr.	F	N	Appendicitis, peritonitis (streptococcus), appendectomy	12/24/30	.....	...	.....	±	0	
5937	6 yr.	F	N	Tuberculosis of lung, miliary tuberculosis	3/ 7/31	3/ 3/31	90	4,272,000	0	0	
5896	9½ yr.	F	W	Hydronephrotic atrophy of kidneys, cardiac hypertrophy, atheroma of aorta	10/ 5/30	10/ 2/30	78	3,032,000	++	±	Blood pressure, 170 systolic and 120 diastolic; 50 per cent dextrose given intravenously; in liver, iron was seen only in an occasional Kupffer cell
5864	11½ yr.	M	W	Tuberculosis of mesenteric glands, miliary tuberculosis of liver, tuberculous meningitis	7/26/30	7/21/30	87	4,256,000	0	0	Elixir ferri given

TABLE 2.—*Iron in the Spleen and Liver in Stillborn Premature Infants*

Autopsy Number	Length	Sex	Race	Diagnosis	Hemosiderosis		Comment
					Spleen	Liver	
1871	27.3	M	W	Prematurity	∓	∓	Very little iron in both organs
1862	27.5	F	W	Prematurity	?	0	Spleen not examined
1888	30.0	F	W	Prematurity, aspiration of amniotic fluid	∓	∓	Rather small amount of iron in both organs
1868	32.5	M	W	Anencephaly, prematurity	∓	∓	Extremely little iron in both organs
1865	35.0	F	W	Prematurity, aspiration of amniotic fluid	∓	0	Very little iron in spleen
1880	35.6	M	W	Prematurity, atelectasis	∓	∓	Very little iron in both organs
1864	39.0	M	N	Congenital syphilis, prematurity	∓	∓	Minimal amounts of iron in liver and spleen
1872	52.5	F	W	Laceration of tentorium, subdural hemorrhage	0	0	Born at full term

TABLE 3.—*Iron in the Spleen and Liver in Very Young Infants*

Autopsy Number	Age	Length	Sex	Race	Diagnosis	Hemosiderosis		Comment
						Spleen	Liver	
1869	4 min.	36.5	M	W	Anencephaly, prematurity	∓	∓	Very little iron in both organs
1902	7 min.	44.0	M	W	Subdural and intracranial hemorrhage, hemorrhage in and about kidneys, prematurity	+	++	Iron in liver cells and bile canaliculi
1883	17 min.	51.0	M	W	Hydrocephaly, spina bifida	+	±	
1891	45 min.	46.0	M	W	Laceration of tentorium, subdural hemorrhage, prematurity	++	±	
1889	1 hr.	53.0	M	N	Laceration of tentorium, subdural hemorrhage	±	+	Blue granules in hepatic cells and bile canaliculi
1897	4 hr.	50.0	F	N	Hemorrhage of lung, aspiration of amniotic fluid	∓	∓	Very little iron in both organs
1845	9.5 hr.	43.0	F	W	Laceration of tentorium, prematurity	∓	±	Very little iron in spleen; iron in liver cells and bile canaliculi
1839	17 hr.	47.0	F	N	Laceration of tentorium, prematurity (slight)	0	0	Only an occasional blue granule in bile canaliculus
1838	22 hr.	46.0	M	W	Prematurity (slight), intracranial hemorrhage, pulmonary hemorrhage	±	0	
1912	1 da.	50.0	F	N	Laceration of tentorium, subdural hemorrhage	0	0	
1840	27 hr.	41.0	M	W	Intracerebral hemorrhage, prematurity	0	0	
1857	35 hr.	32.0	F	W	Prematurity, atelectasis	±	+	
1842	46.5 hr.	28.5	F	N	Prematurity, aspiration of amniotic fluid	+	+	
1844	3 da.	33.2	F	N	Prematurity, atelectasis, hemorrhage of lung, kidney, uterus	+	+	Iron in hepatic cells and bile canaliculi
1833	25 da.	41.0	F	N	Prematurity, abscess of hypogastric artery	++	+	Iron in liver occurred in Kupffer cells

TABLE 4.—*Iron in Liver of Fetuses and Infants*

Autopsy	Age	Length, Cm.	Weight, Gm.	Weight of Liver, Gm.	Moisture in Liver, per Cent	Mg. of Iron per 100 Gm. Whole Liver	Total Iron in Liver, Mg.	Mg. of Hemoglobin Iron per 100 Gm. Whole Liver	Mg. of Nonhemoglobin Iron per 100 Gm. Whole Liver	Total Nonhemoglobin Iron in Liver, Mg.	Mg. of Nonhemoglobin Iron in Liver per Kg. Body Weight	Iron Seen Microscopically	Comment
S. H. Akens	Stillborn	14.0	145	5.0	80.0	17.5 15.7 Av. 16.6	0.83	6.8 6.6 Av. 6.70	9.90	0.495	3.4	0	
L. I. 324	Stillborn	25.0	317	21.6	81.0	26.0	5.62	2.3 2.9 Av. 2.60	23.40	5.054	15.9	0	
S. H. Taylor	Stillborn	32.0	765	39.0	79.0	32.6 38.2 Av. 35.4	13.80	1.97 1.88 Av. 1.93	33.50	13.065	17.1	∓	
B. H. 5994	1 da.	35.0	1,250	32.0	80.0	23.9 31.1 Av. 27.5	8.80	4.74 4.96 Av. 4.85	22.65	7.248	5.8	∓	
S. H. 1955	Stillborn	36.0	785	46.0	80.0	30.8 30.5 Av. 30.7	14.10	2.42 2.32 Av. 2.37	28.33	13.032	16.6	0	
L. I. 325	Stillborn	37.0	1,150	56.0	80.0	22.1 25.9 Av. 24.0	13.40	4.7 5.1 Av. 4.90	19.10	10.696	9.3	0	
S. H. 1948	Stillborn	40.0	1,190	35.5	77.0	23.5 29.9 Av. 26.7	9.48	2.56 2.96 Av. 2.76	23.94	8.499	7.1	0	
S. H. 1953	Stillborn	40.0	3,065	191.0	75.0	40.9 41.5 Av. 41.2	78.69	4.46 4.26 Av. 4.36	36.84	70.364	22.9	±	
S. H. 1952	Stillborn	45.5	1,965	69.0	80.0	30.1 25.3 Av. 27.7	19.11	5.21 5.43 Av. 5.32	22.38	15.442	7.9	∓	
S. H. 1951	Stillborn	45.5	1,765	30.0	83.0	21.0 18.2 Av. 19.6	5.88	1.32 1.15 Av. 1.24	18.36	5.508	3.1	0	
L. I. 293	1 da.	46.0	1,900	66.0	80.0	25.1 25.7 Av. 25.4	16.76	....	.....	.....	....	±	Hemoglobin not determined
S. H. 1950	Stillborn	47.0	2,190	100.0	78.5	21.0 17.9 Av. 19.5	19.50	3.92	15.58	15.580	7.1	±	
S. H. 1949	Stillborn	47.0	3,165	188.5	77.0	78.0 75.5 Av. 76.75	144.67	....	.....	.....	....	+	Hemoglobin not determined; ruptured uterus and hemoperitoneum in mother
L. I. 301	Stillborn	48.0	2,825	116.0	78.0	30.9 27.2 Av. 29.1	33.76	2.51 2.17 Av. 2.34	26.76	31.040	10.9	±	
L. I. 309	54 hr.	50.8	2,600	104.0	76.0	22.5 24.5 Av. 23.5	24.44	17.5 19.0 Av. 18.20	5.30	5.500	2.1	0	
L. I. 306	10 min.	51.2	3,300	138.0	79.0	13.9 12.6 Av. 13.2	18.22	2.86 2.43 Av. 2.64	15.58	21.500	6.5	∓	

S. H. 1947	8 hr.	51.5	3,545	159.0	79.0	36.2 33.5 Av. 34.9	55.50	3.85 4.45 Av. 4.15	30.75	48.900	13.8	±	
L. I. 302	5 min.	52.0	3,300	156.0	76.0	22.5 20.4 Av. 21.4	33.40	2.30 2.48 Av. 2.39	19.01	30.560	9.2	∓	
L. I. 307	Stillborn	54.5	2,700	160.0	79.0	44.1 43.6 Av. 43.8	70.08	10.2 12.8 Av. 11.50	32.30	51.680	19.1	±	
L. I. 303	1 da.	55.5	4,950	288.0	74.0	21.5 20.7 Av. 21.1	60.77	10.8 8.9 Av. 9.90	11.20	32.260	6.5	0	Fatty liver
L. I. 292	6 da.	49.0	2,750	105.0	105.0	80.4 79.6 Av. 80.0	84.00	....	.....	.....	....	+++	Icterus; hemoglobin not determined
L. I. 284	7 da.	52.0	3,700	177.0	76.0	12.3 12.8 Av. 12.5	22.10	1.57	10.93	10.350	5.2	0	Syphilitic hepatitis
B. H. 5990	16 da.	46.0	1,590	75.0	74.0	30.6 37.9 Av. 34.2	25.60	2.14 1.88 Av. 2.01	32.19	24.140	15.3	+	
B. H. 5996	23 da.	41.0	1,390	46.0	77.0	18.8 19.0 Av. 18.9	8.69	2.16 2.12 Av. 2.14	16.76	7.710	5.5	∓	
B. H. 5987	2.5 mo.	61.0	5,530	286.0	77.0	38.3 41.6 Av. 40.0	114.00	4.50 1.74 Av. 3.12	36.88	105.480	19.1	+	

Hueck [3] found that the adult liver washed free from blood contained on the average about 50 mg. of iron per hundred grams of dried substance. Nevertheless, by the method used, little or no iron was histologically demonstrable in the normal adult liver. Hueck found, however, that with an increasing abnormal amount of iron in the liver, the amount demonstrated histologically increased, and that the two ran parallel.

Since the work of Bunge [4] and Zaleski,[5] the general thesis has been held that the fetus accumulates iron during intra-uterine life to compensate for the low iron content of breast milk which alone forms the diet of the nursling. Since the highest amounts of iron were seen in our patients not immediately after birth but from one to ten weeks later, we were compelled to reexamine this thesis. Histologic study of the liver in a series of stillborn infants from the fifth to the tenth months of intra-uterine life (table 2), and also in a series of new-born infants during the first thirty-six hours of life (table 3), gave no evidence of large or progressive accumulations of iron. Because of the unexpected result of these studies and because of the heterodox nature of the conclusions reached, it seemed advisable to supplement the histologic studies with chemical analyses for iron in a series of livers. Both chemical and histologic studies were made of the iron content of the livers of human fetuses and infants from the fourth month of intra-uterine to the third month of postnatal life (table 4). Chemical analyses for iron were also made on several samples of livers preserved in formaldehyde taken from cases that had previously been studied histologically (table 5). These studies support the conclusions reached on histologic grounds, and offer quantitative data of considerable significance.

CASES IN WHICH TRANSFUSION OF BLOOD WAS MADE

In the first group of one hundred cases studied, transfusions of blood had been given during life in thirty, and in practically all of these, iron was found microchemically in moderate amounts in the liver and in abundant amounts in the spleen. The rôle of the spleen in the destruction of transfused erythrocytes [6] has been experimentally demonstrated in animals and is indicated by the observations in human beings here reported.

The presence of iron was demonstrated and its amount estimated microscopically in paraffin sections stained with an acidified solution of potassium ferrocyanide and counterstained with fuchsin.[2]

3. Hueck, W.: Beitr. z. path. Anat. u. z. all. Path. **54**:68, 1912.

4. Bunge: Lehrbuch der physiologischen und pathologischen Chemie, ed. 2, Leipzig, F. C. W. Vogel, 1889.

5. Zaleski: Ztschr. f. phys. Chem. **10**:453, 1886.

6. Kühl, G.: Ergebn. d. inn. Med. u. Kinderh. **34**:302, 1928.

Since iron is demonstrable in the liver and spleen of many infants during the first three months of life, this age group (of thirteen cases) did not help particularly in the study of the histologic changes produced by transfusions of blood per se. These cases are therefore separately

TABLE 5.—*Iron in the Liver* of Infants and of Adults*

Autopsy	Age	Diagnosis	Moisture in Liver, per Cent	Weight of Liver, Gm.	Mg. of Iron per 100 Gm. of Liver	Total Iron in Liver, Mg.	Iron Seen Microscopically	Comment
B. H. 5929	3 wk.	Bronchopneumonia, acute glomerulonephritis	75	160	82.7 65.0 Av. 73.8	118.1	++	No transfusions of blood
B. H. 5935	1 mo.	Intestinal intoxication, subacute pancreatitis	75	84	81.5	68.0	+	No transfusions of blood
B. H. 5835	5 wk.	Hemorrhage into cerebral ventricle, icterus	65	92	115.3 165.5 Av. 140.4	129.2	+++	No transfusions of blood
B. H. 5831	41 da.	Prematurity, icterus	72	80	234.0 178.5 Av. 206.2	165.0	+++	No transfusions of blood
B. H. 5900	2 mo.	Bronchopneumonia, edema of lungs	..	148	32.0	47.4	+	No transfusions of blood
B. H. 5928	4 yr.	Bronchopneumonia, suppurative pleurisy	77	...	14.0 9.8 Av. 11.9	.....	0	No transfusions of blood
B. H. 5916	5 yr.	Tuberculous pneumonia, miliary tuberculosis	74	650	21.0 13.0 Av. 17.0	110.0	0	No transfusions of blood
P. H. 10309	13 yr.	Tetanus	67	1,100	25.7	283.0	0	
P. H. 10334	20 yr.	Bronchopneumonia	70	1,440	28.9	416.0	0	
P. H. 10348	33 yr.	Bronchial asthma	..	.....	39.0	.....	0	
P. H. 10373	50 yr.	Lobar pneumonia	68	1,800	38.0	684.0	0	
P. H. 10301	62 yr.	Carcinoma of urinary bladder	70	2,300	33.6	773.0	0	
B. H. 5865	3 yr.	Agranulocytosis, secondary anemia	76	.....	102.4 107.9 Av. 105.2	.....	+++	Nine transfusions of blood to total of 1,760 cc.
P. H. 10336	44 yr.	Hemorrhage into cerebrum	65	2,160	71.6	1,547.0	+	
P. H. 10568	38 yr.	Secondary anemia	..	1,660	203.0	3,370.0	+++	20 transfusions of blood to total of 12,440 cc.; splenectomy
P. H. 10522	29 yr.	Acquired hemolytic jaundice	..	1,950	472.0 476.0 Av. 474.0	9,243.0	++++	17 transfusions of blood to total of 10,030 cc.

* Chemical estimate was made of small pieces of liver that had been preserved in formaldehyde for various lengths of time.

listed (table 6). In this group the very large amounts of iron in the liver and spleen depend on postnatal destruction of blood (see the following), on transfusions of blood and in some cases on hemorrhage resulting from injuries received at birth. Since in this group the causes of hemosiderosis are multiple or cumulative, the effectiveness of any particular one is difficult of evaluation. The following groups are more informative.

TABLE 6.—*Transfusions of Blood in Patients Under Three Months of Age Arranged in Order of Age*

Autopsy Number	Age	Sex	Race	Diagnosis	Autopsy Date	Blood			Transfusions of Blood			Hemosiderosis		Comment
						Date	Hemoglobin	Red Blood Cells	Date	Amount	Interval*	Spleen	Liver	
5813	13 da.	F	W	Meningeal hemorrhage, pneumococcus bacteremia, suppurative periarthritis	4/21/30	4/ 3	128	4,976,000	4/16 4/18	60 60	3	+++	++	
5850	16 da.	F	W	Congenital atresia of esophagus, hemorrhagic disease of new-born	7/ 2/30	6/22	125	5,176,000	6/22 6/23	30 65	9	++	+	Icteric index, 50; iron in liver cells
5917	1 mo.	M	W	Staphylococcus septicemia, icterus	12/ 9/30	11/20	155	5,168,000	11/21 12/ 7	80 60	2	+++	++	Abundant iron in Kupffer cells; most of pigment in hepatic cells did not take iron stain
5807	5 wk.	M	W	Intestinal intoxication (clinical), pulmonary congestion, fatty liver	4/11/30	2/15	119	5,048,000	2/15 3/15	80 70	27	+++	++	
5836	1½ mo.	F	W	Undescended cecum, pericecal abscess, peritonitis	6/ 4/30	5/12	120	4,752,000	5/28 5/29 6/ 2	70 60 80	2	+++	+	Iron in Kupffer cells
5856	1½ mo.	F	W	Omphalitis, biliary cirrhosis of liver, septicemia (hemolytic streptococcus)	7/11/30	7/ 2	40	1,616,000	7/ 5 7/ 9	75 62	2	++	++	Iron present in both Kupffer and hepatic cells
5903	7 wk.	M	W	Prematurity, bronchopneumonia, congenital syphilis	11/ 1/30	10/27	110	4,530,000	10/25	60	7	++	+	In liver, very little iron in hepatic cells; considerably more in Kupffer cells
5812	7 wk.	F	W	Pseudohermaphroditism, hypertrophy of suprarenals, visceral congestion	4/21/30	3/29	100	5,250,000	3/30	80	22	+++	++	Dextrose and saline solution given intravenously
5869	2 mo.	M	W	Cardiospasm, bronchopneumonia	8/ 5/30	7/31	73	3,280,000	7/31 8/ 4	60 60	1	+++	++	In liver, most of iron in Kupffer cells; a small amount in hepatic cells
5861	2 mo.	M	W	Bronchopneumonia, otitis media	7/20/30	6/30	114	4,656,000	7/ 7	60	13	+	++	Iron present in both Kupffer and hepatic cells
5808	2 mo.	M	W	General icterus, erysipelas, bacteremia (hemolytic streptococcus)	4/11/30	3/26	66	3,408,000	3/28	90	14	±	±	Dextrose and saline solution given intravenously, 200 cc., van den Bergh reaction, positive
5810	2 mo.	F	W	Congenital syphilis, cystic ovary	4/16/30	4/13	66	2,760,000	?	?	?	++	++	Intraperitoneal transfusion of blood; viosterol given
5800	9 wk.	M	W	Hyperplasia of thymus, catarrhal colitis	4/ 2/30	3/19	104	4,504,000	3/20 3/29	60 80	4	+++	+	

* The number of days between the last transfusion of blood and the date of autopsy.

TABLE 7.—*Repeated Transfusions of Blood in Patients Over Three Months of Age, Arranged in Order of the Number of Transfusions*

Autopsy Number	Age	Sex	Race	Diagnosis	Autopsy Date	Blood			Transfusions of Blood			Hemosiderosis		Comment
						Date	Hemoglobin	Red Blood Cells	Date	Amount	Interval*	Spleen	Liver	
5815	3 mo.	M	W	Pachymeningitis hemorrhage interna, bronchopneumonia, otitis media	4/26/30	3/13	77	4,432,000	4/ 4 4/18	80 100	8	+++	++	Much iron in both Kupffer and liver cells
5848	3 mo.	F	W	Omphalitis, peritonitis (streptococcus hemolyticus), erysipelas	6/28/30	6/14	43	2,212,000	6/14 6/21	100 80	7	++	±	
5859	9½ mo.	M	W	Acute otitis media, multiple ulcers of small intestine	7/15/30	7/ 1	92	5,856,000	7/ 7 7/10 7/12	100 80 80	3	+	+	
5825	11 mo.	F	W	Erysipelas, fatty liver, bacteremia (hemolytic streptococcus)	5/15/30	5/ 9	51	3,846,000	5/10 5/12 5/14	120 120 120	1	++	∓	Very little iron in liver
5871	8½ mo.	F	W	Suppurative pleurisy, ulcers of small intestine	8/10/30	7/ 4	58	3,064,000	7/ 8 7/26 7/31 8/ 5	80 100 100 120	5	+++	+	Numerous clyses and infusions; also dextrose given intravenously
5858	6½ mo.	F	W	Bronchopneumonia, edema of pia	7/12/30	5/ 7	70	4,912,000	5/ 8 5/17 6/13 7/ 8 7/11	100 100 100 80 140	1	+++	++	Iron present in both Kupffer and hepatic cells
5923	3 yr., 3 mo.	M	W	Miliary tuberculosis, secondary anemia, hyperplasia of bone marrow	1/ 3/31	5/28 5/31 10/ 8	25 45 90	1,280,000 2,428,000 4,328,000	5/29 6/10 6/17 6/23 11/22 11/27 12/16	200 240 250 190 150 220 180	18	++	+	Albuminized iron in diet; in liver, iron present in both Kupffer and hepatic cells
5877	3½ yr.	M	W	Acute lymphatic leukemia, splenomegaly	8/28/30	4/12 8/26	38 49	1,640,000 2,590,000	4/14 4/22 4/30 8/15 8/23 8/24 8/25	? ? ? 150 200 100 100	3	++	+	In liver, iron present in both Kupffer and hepatic cells
5865	3 yr.	M	W	Agranulocytosis, gangrenous pharyngitis, hypoplasia of bone marrow, hemolytic streptococcus bacteremia, secondary anemia	7/28/30	4/21 4/27 7/26	17 43 65	800,000 2,784,000 3,528,000	4/21 4/24 4/30 7/21 7/22 7/23 7/24 7/25 7/26	200 200 200 200 200 200 200 120 140	2	++	+++	Iron of liver almost entirely in Kupffer cells; albuminized iron and liver in diet

* The number of days between the last transfusion of blood and the date of autopsy.

TABLE 8.—*Single Transfusions of Blood in Patients Over Three Months of Age Arranged in Order of Interval of Time Between Transfusion and Autopsy*

Autopsy Number	Age	Sex	Race	Diagnosis	Autopsy Date	Blood			Transfusions of Blood			Hemosiderosis		Comment
						Date	Hemoglobin	Red Blood Cells	Date	Amount	Interval*	Spleen	Liver	
5822	10 yr.	F	W	Suprapubic cystotomy, suppurative nephritis, dilatation of gallbladder	5/11/30	4/23	95	5,024,000	5/10	225	18 hr.	+++	∓	Very little iron in liver
5830	7½ yr.	F	N	Suppurative pleurisy, purulent peritonitis (streptococcus)	5/26/30	5/14	60	3,928,000	5/24	100	2 da.	++	±	
5878	6 mo.	M	W	Intestinal intoxication, ulcer of small intestine	8/29/30	8/ 5	83	4,580,000	8/27	90	2 da.	±	+	In liver, iron found almost exclusively in hepatic cells
5911	1 yr.	F	W	Congenital malformation of bladder, hydronephrosis, operation: ureterostomy	11/28/30	10/ 7	68	3,820,000	11/25	?	3 da.	+	+	Viosterol given
5876	5 mo.	M	W	Intestinal intoxication (clinical)	8/25/30	8/ 6	83	4,270,000	8/21	80	4 da.	++	++	Iron present in both Kupffer and hepatic cells
5899	6 mo.	M	W	Intestinal intoxication (clinical), atelectasis of lungs	10/11/30	10/ 7	100	4,344,000	10/ 7	100	4 da.	+	+	2,000 cc. saline solution and dextrose given by infusion during 4 days in hospital
5904	15 mo.	M	W	Bronchopneumonia, secondary anemia, prematurity	11/ 5/30	10/28	20	2,128,000	10/31	120	5 da.	+	±	Liver and albuminized iron in diet
5866	4 mo.	M	W	Intestinal intoxication (clinical), bronchopneumonia	7/28/30	7/23	135	7,456,000	7/21	80	7 da.	+	+	Liver pigment in hepatic cells; granules in portal areas blue; those in central areas red

* The time between the transfusion of blood and the date of autopsy.

Of the seventeen patients 3 months of age or older, nine had received more than one transfusion of blood (table 7), and eight had received only one (table 8). In the latter group the findings are significant, since they point out with regard to human beings not only the histologic changes after a single transfusion, but also how quickly these changes occur. In three patients, death occurred within two days after transfusion. Abundant iron was found microscopically in the spleen (+++, ++, ±); smaller amounts were seen in the liver (∓, ±, +). From the third to the seventh day after a single transfusion, iron was found in both the liver and the spleen, but the spleen appeared to contain less than on the second day, while the liver appeared to contain more.

Appropriation and Utilization of Transfused Blood.—Experimental work and clinical observations on the transfusion of blood were summarized by Kühl,[6] who also reported his own illuminating experiments. He bled rabbits and then gave them transfusions of an equivalent amount of blood from other rabbits. The transfused erythrocytes were found to be removed from the circulating blood within eight hours. In rabbits previously splenectomized this time was prolonged to seventy-two hours. "Blockade of the reticulo-endothelial system" by the intravenous injection of dyes produced a similar delay. In anemic animals transfused blood was removed in from twenty-four to forty-eight hours. How then can the beneficial results of transfusions be explained? Kühl rejected the theory that the benefit arises from a substitution of foreign blood in place of the blood that the patient lacks, because transfused erythrocytes quickly disappear from the recipient's circulating blood. He rejected the idea of stimulation of bone marrow largely because in pernicious anemia, in which the bone marrow is hyperplastic, the provision of more stimulus by transfusion of blood would be illogical. He concluded that the benefit of transfusions results from a "blockade of the reticulo-endothelial system" which is so taken up with the destruction of the transfused cells that the recipient's own cells are spared. Since the formation of blood in the marrow continues while the recipient's erythrocytes are not subject to the usual destruction, the red count rises, and the benefits are clinically manifest. The primary effect is a blockade of the reticulo-endothelial system. Only secondarily can the transfusion stimulate the bone marrow by the products of destruction of the red cells.

Especially significant is the work of Ashby,[7] who studied the length of life of transfused blood corpuscles in man by using serums that agglutinated the recipient's erythrocytes but did not affect the transfused cells. Ashby found that "the life of the transfused cell is long; it has been found to extend for thirty days and more." Of the seven

7. Ashby: J. Exper. Med. **29**:267, 1919.

cases studied, complete protocols were reported in three. In two of these the erythrocyte count for transfused cells was reduced by 50 per cent during the first two weeks after tranfusion. Nevertheless, the "duration of life" of transfused cells for human beings as reported by Ashby was considerably longer than that for rabbits as reported by Kühl.

Regarding human beings, the histologic studies here reported suggest the following mechanism. Transfused erythrocytes to a considerable (but as yet quantitatively undetermined) extent are phagocytosed by the cells of the reticulo-endothelial system of the recipient. This phagocytosis occurs predominantly in the spleen. That transfused cells are destroyed more rapidly than normal cells is indicated by the abnormal amount of phagocytosed red cells in the spleen of patients who have been given transfusions shortly before death. This is strikingly illustrated in case 5822, a girl of 10 who died of suppurative nephritis and who had received a transfusion of 225 cc. of blood about eighteen hours before death (table 8). Such findings are not in keeping with the idea that the effectiveness of transfusions depends on a transplant of viable cells. Nevertheless, it is quite conceivable that the longevity of transfused cells will be affected by the limited capacity of the reticulo-endothelial system to destroy them, a factor that Kühl emphasized. We do not feel that a "blockade of the reticulo-endothelial system" can play more than a transient rôle, because the phagocytes of the spleen are aided by those in the liver, lymph glands, suprarenals, bone marrow and endothelial cells throughout the body. These cells show a tremendous capacity for increasing in numbers and for loading themselves with foreign cells, dyes, particulate matter, etc. They respond to increased demands by increasing in size and number, and consequently by an increase in capacity for work. Large, frequently repeated transfusions of blood would thus lead to a "hypertrophy of the reticulo-endothelial system."

It appears, therefore, that in human beings at least part of the transfused blood is quickly phagocytosed. The red cells are physically disintegrated and chemically digested within the phagocytes, and the products are liberated into the blood stream. Among these products are the bilirubin and iron derived from the hemo portion of the hemoglobin, and the poorly known but possibly extremely important derivatives of the globin portion of the molecule. Our findings indicate that in large amounts iron as well as bilirubin is taken up from the blood stream by the hepatic cells. That the kidney removes large quantities of urobilin under these circumstances has been demonstrated. The kidney, furthermore, has the power of taking up iron from the blood stream after extensive destruction of blood, and this iron may be found in the urine.

Shortly after a transfusion of blood there appear in the blood plasma of the recipient the products of disintegration of the donor's cells, which products are identical with or similar to the construction materials of the recipient's red cells. The fate of these products will depend on various factors—the need of the recipient for new erythrocytes, the suitability of these products as construction materials in hematopoiesis, the ability of the bone marrow to carry on its blood-forming function, and, of particular importance, to my mind at least, the relation between the rate at which the building materials are liberated into the blood stream and the rate at which the bone marrow can utilize them. It seems probable that after large, frequently repeated transfusions of blood, the catabolic changes in the blood-destroying phagocytes are more rapid than the anabolic changes in the blood-forming cells of the bone marrow. The mechanism as here interpreted suggests that transfusion of blood is a specialized form of parenteral feeding rather than a direct substitution for missing blood. It follows that frequently repeated transfusions of large amounts of blood will liberate into the blood plasma the building stones of hemoglobin more rapidly than the bone marrow can utilize them, with a loss of at least part of the surplus in the excretions of the body. It is possible, therefore, that a given amount of blood when transfused for the purpose of improving a patient with anemia, and when there is no question of increasing the blood volume to combat shock, will be best utilized by the recipient when given in fairly small amounts at least several days apart. A more accurate specification of amount and frequency must rest on clinical trial.

IRON IN THE LIVER

If one tabulates in the order of the age of the patients the seventy cases in which no transfusions had been given, it becomes apparent that with the completion of the third month of life, there is a definite decrease in the amount of iron seen microscopically in both spleen and liver (table 1). Hugounenq,[8] in 1899, made determinations of the total iron (Fe_2O_3) content of the fetus and new-born child and reported the following figures: at 5½ months, 0.126 Gm.; at 6 months, 0.119 Gm.; at term, 0.383 Gm. and at term, 0.421 Gm.

It is apparent that the acquisition of iron in the fetus is greater during the last four months of intra-uterine life than during the first six.

Bunge [4] pointed out that the iron content of the liver in the new-born animal is from five to nine times as great as that in the adult. This conclusion is based on the determinations of iron in the livers of dogs

8. Hugounenq: Compt. rend. Soc. de biol. **51**:337, 1899.

reported by Zaleski:[5] new-born dog, 0.3907 per cent of iron in dried substance; adult dogs, 0.0891, 0.0779 and 0.0429.

Bunge also demonstrated the low iron content of milk, and stated that iron is stored in the liver during fetal life to meet the needs of the infant during the first few months after birth, when the diet consists of mother's milk, which has a low iron content. Our own histologic observations do not entirely support this idea, and have led us to a hypothesis that is somewhat different. It may be stated as follows: The iron contents of the spleen and liver of human beings reach their maximum, not at birth, but from one to ten weeks after birth, and the large amounts of iron seen in these organs result, not from accumulation during intra-uterine existence, but from the destruction of blood that occurs in the infant shortly after birth.

To return to the evidence already presented as forming the basis for the idea of the storage of iron in the liver during fetal life, it should be noticed that the figures of Hugounenq represent the total iron con-

TABLE 9.—*Iron in the Liver of Rabbits*

Number	Age	Weight, Kg.	Iron in Blood per 1,000 Cc.	Weight of Liver, Gm.	Iron in Washed Liver per 1,000 Gm.
1	8 da.	0.120	0.45	4.06	1.000
2	11 da.	0.137	0.40	4.10	0.200
3	21 da.	0.320	0.41	10.00	0.140
4	3 mo.	1.170	....	90.00	0.043
5	3 mo.	1.350	0.42	105.00	0.035
6	3 mo.	1.360	0.36	72.00	0.040

tent of the fetus at various ages; furthermore, that the gain in total weight during the last three months of fetal life is greater than the gain during the first seven, so that during either period of intra-uterine life the increase in total iron is not more marked than the increase in total weight.

We have made histochemical studies of the livers of eight stillborn fetuses (table 2) varying in length from 27.3 cm. to 52.5 cm. (i. e., from about five to ten months of fetal life), and we have found no evidence to support the idea of large or progressive depositions of iron in the liver during intra-uterine life. That iron is present in small or moderate quantities we have no doubt, but these are smaller than the quantities of iron found from the second to the tenth week of extra-uterine life.

Lapicque[9] studied the iron content of the liver in young rabbits. His results are given in table 9. He thought that perhaps the first figure for iron in the liver was incorrect because it is so large. Despite this fact, we are inclined to believe that the figure is no less accurate than those that follow. The important point is that the high iron content of the

9. Lapicque, M. L.: Compt. rend. Soc. de biol. **1**:510, 1889.

liver is found not in a new-born rabbit but in one 8 days old, i. e., after the postnatal destruction of blood is well under way. Lapicque also made determinations of the iron content of the organs of a litter of six female puppies who were drowned a few hours after birth. These figures follow:

Organ	Average Weight	Iron per 1,000 Gm.
Spleen	1.0 Gm.	0.14
Liver	40.0 Gm.	0.17
Thymus	1.7 Gm.	0.04
Long bones	6.0 Gm.	0.08

It is apparent that the iron in the liver of rabbits 8 days old is about six times as concentrated as that in the liver of puppies "a few hours" after birth.

Chemical Analysis of Human Livers for Iron.—A series of twenty-five fresh livers obtained at necropsies of fetuses and infants were analyzed for iron and for hemoglobin. A number of livers preserved in formaldehyde were also available from cases previously studied. Samples of these were analyzed chemically for iron. The moisture content was calculated from the loss of weight of a small sample after twenty-four hours in the oven at 80 C.

Technic.—Estimation of Hemoglobin: A portion (from 1 to 3 Gm.) of liver, finely minced and thoroughly mixed, was weighed in a 50 cc. volumetric flask. Distilled water was added, and the flask was vigorously shaken. It was then put in the refrigerator over-night. The following day the contents were filtered. To 10 cc. of the filtrate was added 4 drops of concentrated hydrochloric acid. After standing for two hours, the results were read in the colorimeter against the Newcomer standard hemoglobin disk.[10] The concentration of iron in hemoglobin was taken as 0.335 per cent.

Estimation of Iron: The method of Kennedy[11] was followed exactly, except for the preparation of the ash. Instead of wet ashing with perchloric acid, the liver was dry ashed, the final oxidation being effected with a few cubic centimeters of concentrated nitric acid.

In the preserved specimens, determinations of hemoglobin were not attempted. No account was taken of possible change in weight of the liver due to the preservative. Several preserved specimens resisted complete dry ashing, which might tend to give underestimations. The resistant ashes were extracted with nitrohydrochloric acid.

Results.—To obtain an estimate of the amount of iron in the hepatic and Kupffer cells, the hemoglobin iron was subtracted from the total amount of iron, the difference being expressed as milligrams of non-hemoglobin iron per hundred grams of whole liver (table 4). The findings do not indicate a progressive rise in that figure during the latter half of fetal life. The average nonhemoglobin iron content of the whole liver among the seven most mature infants under 3 days of age

10. Newcomer: J. Biol. Chem. **55**:569, 1923.
11. Kennedy: J. Biol. Chem. **74**:385, 1927.

was 32 mg. Even if all this iron were available for the formation of hemoglobin it would be sufficient to account for only 64 cc. of new blood.

In only one liver was the iron content surprisingly large (S. H. 1949). This baby was removed from the ruptured uterus of a woman who had had a previous cesarian section. At operation the mother presented an extensive hemoperitoneum. Iron liberated from the extravasated blood probably reached the fetal liver through the placenta. Similarly, it is highly probable that in other cases in this series part of the iron in the liver was due to hemorrhages in the mother, the baby or both.

The marked hemosiderosis of the liver seen microscopically in many infants from the second to the tenth week of postnatal life is paralleled by the observations on chemical analysis of samples of these livers (table 5). The highest figure is seen in B. H. 5831, a premature icteric infant who died at the age of 41 days. Allowing for the iron present in the liver at birth, the excess indicates a destruction of at least 200 cc. of blood and probably more. This amount approaches the total blood volume of the premature infant at birth. It should be noted, however, that in some of the cases within this age group, there was only a moderate increase or none in the iron content of the liver, either microscopically or chemically. If the hemosiderosis of the liver is related to postnatal destruction of blood, and the histologic appearances strongly support this view, it must be assumed that the extent and rapidity of the destruction of blood vary in different infants.

Destruction of Blood in Infants.—The concentration of hemoglobin in the blood of infants shows a progressive decrease during the first three months of life. Williamson [12] reported hemoglobin to be 178 per cent in infants 1 day old, as compared to 104 in infants from 3 to 5 months of age. Appleton [13] found a progressive decrease in the percentage of hemoglobin in the blood from 164 at birth to 88 at 3 months of age and a very slight decrease thereafter. Goldbloom and Gottlieb [14] reported a progressive fall in the red cell count of an infant from 6,900,000 to 4,250,000 during the first one hundred and eight hours of life. One must bear in mind that the normal infant doubles his birth weight in about fourteen weeks, and that undoubtedly there is a concomitant increase in blood volume. This in itself would tend to show lower readings for hemoglobin at 14 weeks of age if the growth in the number of red cells lagged behind the growth of the rest of the body. It could not, however, explain the progressive fall in hemoglobin during the

12. Williamson, C. S.: Influence of Age and Sex on Hemoglobin, J. A. M. A. **65**:302 (July 24) 1915.

13. Appleton: J. Biol. Chem. **34**:369, 1918.

14. Goldbloom, A., and Gottlieb, R.: Icterus Neonatorum, Am. J. Dis. Child. **38**:57 (July) 1929.

first week or two of life. This fall in the red cells, together with visible icterus which appears at the same time and Schiff and Faerber's [15] demonstration of bilirubinemia (indirect van den Bergh) in all newborn infants, are sufficient clinical evidence that there is active destruction of blood. The histopathologic changes associated with this intravascular destruction of blood are identical with the changes that we

TABLE 10.—*Bunge's Comparison of Total Iron Content in Guinea-Pigs and Rabbits*

	Guinea-Pigs			Rabbits			
	Body Weight, Gm.	Iron Content, Mg.	Mg. of Iron per 100 Gm. of Body Weight		Body Weight, Gm.	Iron Content, Mg.	Mg. of Iron per 100 Gm. of Body Weight
Embryo	16.6	0.8	4.6	Embryo	7.8	0.5	6.4
	32.3	1.4	4.4		15.3	1.3	8.5
	43.6	2.5	5.6		33.5	3.0	9.0
	64.3	3.4	5.3				
	94.4	4.7	5.0				
New-born	101.8	5.8	6.0	New-born	59.3	9.5	18.2

TABLE 11.—*Abdehalden's Figures for Hemoglobin and Iron in Young Rabbits*

		Weight of Hemoglobin, Gm.		Total Weight of Iron, Mg. in Body			Mg. of Iron per 1,000 Gm. of Body Weight		
A.	*B.*	*C.*	*D.*	*E.*	*F.*	*G.*	*H.*	*I.*	*K.*
Age, Days	Weight of Animal, Gm.	In Entire Body Minus Intestine	Per 1,000 Gm. of Body Weight	In Hemoglobin	Not in Hemoglobin	Sum of Both	In Hemoglobin	Not in Hemoglobin	Sum of Both
1	54	0.675	12.61	2.27	5.23	7.5	42	97	139
3	64	0.699	10.91	2.35	3.95	6.3	37	62	99
4	...	.....	.....	....	.....		..		
6	115	0.760	6.61	2.55	7.25	9.8	22	63	85
10	159	0.773	4.87	2.59	.....	....	16	27	43
11	...	.....	.....	....	.....	....	..		
13	...	.....	.....	....	.....	....	..	32	45
14	258	0.981	3.81	3.30	8.30	11.6	13		
17	...	.....	.....	....	.....	....	..	32	43
18	352	1.096	3.21	3.68	.....	....	11		
22	466	1.122	2.41	3.78	16.22	20.0	8	35	43

found associated with the destruction following transfusions, namely phagocytosis of erythrocytes by the cells of the reticulo-endothelial system, predominantly in the spleen, with iron in the hepatic cells and, when abundant, in the bile canaliculi. Altered or broken down red cells or their products may reach the blood stream from hemorrhages due to birth injuries. In particulate form, these are taken up by the cells of the reticulo-endothelial system; if the iron from such a hemor-

15. Schiff and Faerber: Jahrb. f. Kinderh. **97**:245, 1922.

rhage is separated and gets into the blood stream in dissolved form, it will be largely taken up by the hepatic cells of the cord of the liver.

A histologic study of iron in the liver and spleen of infants was made in 1924 by Schwartz, Baer and Weiser.[16] Their observations as regards the age groups are similar to our own in all essential respects. They were particularly interested in premature infants, because they show a greater frequency and severity of anemias, but the authors could find no cause for separating the premature infants from those born at term.

IRON METABOLISM AND HEMATOPOIESIS IN THE FETUS AND INFANT

The study of iron in the spleen and the liver has a direct bearing on the questions of iron metabolism and hematopoiesis in fetuses and infants (as well as in adults) and on the anemias of early life.

Bunge[17] reported the total iron content of guinea-pig and rabbit fetuses, and his results are given in table 10. He pointed out the much higher content of iron in rabbit fetuses, and added the following observation to explain it: "Rabbits are blind at birth, have very little hair, are awkward in their movements, and have to remain in warm nests for two weeks. Guinea-pigs are born with eyes open, and thick warm furs; they run about within a few hours and seek their own nourishment." The guinea-pig very soon eats iron-containing vegetables, while the new-born rabbit lives on milk, which is poor in iron.

An idea of the changes in iron and hemoglobin characteristic of early life may be obtained from the figures of Abderhalden[18] for rabbits (table 11). Bunge determined the total iron content of the bodies of young rabbits as recorded in column *K*. Abderhalden determined the total hemoglobin content of the bodies of young rabbits as recorded in column *C*. From these figures, he calculated the iron in the hemoglobin of the animals as well as the surplus nonhemoglobin iron per thousand grams of body weight. From Abderhalden's figures regarding total hemoglobin and hemoglobin per thousand grams of body weight as recorded in columns *C* and *D*, we calculated the weights of the animals and then the total iron in the body of each. We then calculated the iron in the total hemoglobin of each animal (column *E*), using 0.336 per cent as the concentration of iron in rabbits' blood.[18] The figures in column *F* represent the difference between columns *E* and *G*.

16. Schwartz; Baer, and Weiser: Ztschr. f. Kinderh. **37**:167, 1924.

17. Bunge, G.: Ztschr. f. phys. Chem. **17**:63, 1893.

18. Abderhalden: Lehrbuch der physiologischen Chemie, Berlin, Urban & Schwarzenberg, 1906.

Certain interesting changes may be observed in these figures. On the sixth day the rabbit has doubled his birth weight, yet the total hemoglobin has increased by only 13 per cent; accordingly, the percentage of hemoglobin with regard to body weight has been reduced almost to half. There can be no question that the total blood volume has increased with the body weight (perhaps not as a linear function), and that the percentage of hemoglobin per unit volume of blood has fallen considerably.

Changes of total hemoglobin in the blood of an animal depend only on two factors: the rate of formation of new blood and the rate

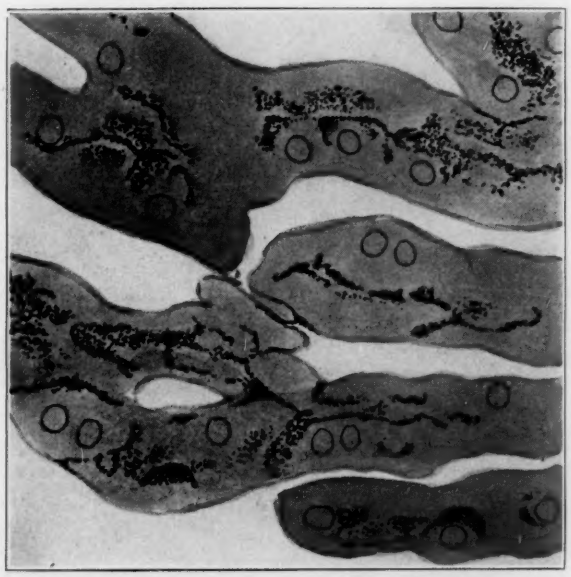

Fig. 1 (case 5929).—Drawing of the liver. Stained for iron with potassium ferrocyanide; fuchsin counterstained. Oil immersion objective; ocular 10 ×. Note the iron in bile canaliculi and in the cytoplasm of the liver cells adjoining them. (Drawing by Mr. Alfred Feinberg.)

of destruction or loss of blood. Changes in the percentage of hemoglobin depend on these two factors as well as on a third, the total blood volume. It is apparent, therefore, that if an infant's blood volume doubles with his birth weight within fourteen weeks, the total hemoglobin may remain unchanged, yet the percentage of hemoglobin per unit volume of blood will be reduced by half. Attending and following the destruction of blood in early life there unquestionably is a rapid formation of blood. The destruction of blood that begins so soon after birth accounts for the large quantities of iron to be found in the liver

and the spleen from the second to the tenth weeks of life. This rapid destruction of blood quickly abates, however, but the increasing total hemoglobin demonstrates the continued high level of activity of the bone marrow, which uses as building stones the products of destruction of the red cells. With the marked slowing of destruction of blood and the continuation of rapid formation of blood, the great excess of iron in the spleen and liver disappears. Our studies indicate that in human beings this occurs during the fourth month of life. The abundance of hepatic iron during the first three months of life perhaps explains the finding of Silberschmidt [19] that the feeding of an iron preparation

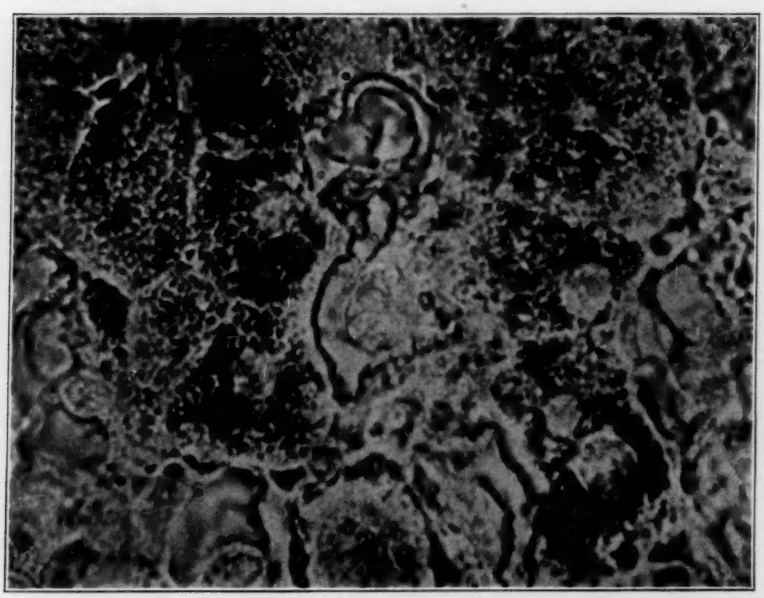

Fig. 2 (case 5929).—Photomicrograph of the liver. Stained for iron with potassium ferrocyanide; very faint picric acid counterstain. Dark masses indicate prussian blue reaction; × 1,680.

during the first three months of life did not prevent the development of anemia in premature infants.

It is probable, therefore, that large amounts of iron are seen in the spleen and the liver as a result of rapid destruction of blood, and that the same iron may be utilized by the bone marrow in the formation of new blood. The premature infant is born with a smaller blood volume and a smaller total iron content than the child born at term. Milk as a source of food is the same for both. The essential difference is that the premature child has been deprived of the abundant iron and other

19. Silberschmidt: Jahrb. f. Kinderh. **129**:63, 1930.

blood-forming elements that would have been derived from the mother by way of the placenta during the last two or three months of intrauterine life. This handicap need not show itself in blood counts made early in life, but accounts for the lower hemoglobin readings at the age of 3 months for premature children as compared with those born at term. The premature infant starts with a smaller reserve and exhausts it more quickly. Hence anemia in premature children will appear earlier and will be more severe than in children born at term. Likewise supplementary feeding of an iron preparation will be necessary earlier for premature infants than for those born at term.

Fig. 3 (case 5876).—Photomicrograph of the spleen; potassium ferrocyanide and faint picric acid stains; × 160. Note the abundant iron.

When iron is brought to the liver in large quantities after extensive destruction of blood, it can be seen in the bile canaliculi and in the cytoplasm of the hepatic cells bordering them (fig. 1). Normally, iron is excreted in the bile in small amounts.[20] After extensive destruction of blood a copious excretion of iron by way of the liver may occur, as is indicated by our microscopic observations. This results from the inability of the bone marrow to utilize the products of destruction of the red cells at the extremely rapid rate with which they are

20. Dominici: Arch. per le sc. med. **53**:390, 1929.

formed. Accordingly, Langstein and Edelstein [21] found that a newborn infant during the first two days of life, when nourishment was practically nil, lost 2 mg. of iron in the stools. The iron balance continued to be negative during the next five days, but then became positive. The loss of iron during the first twenty-four hours of life in the rabbit is perhaps too strikingly illustrated by the observations of Bunge, who reported 18.2 mg. of iron per hundred grams of body weight in a rabbit one hour after birth as compared with 13.9 mg. in a rabbit 1 day old. From the figures in columns *E* and *F* it can be seen that

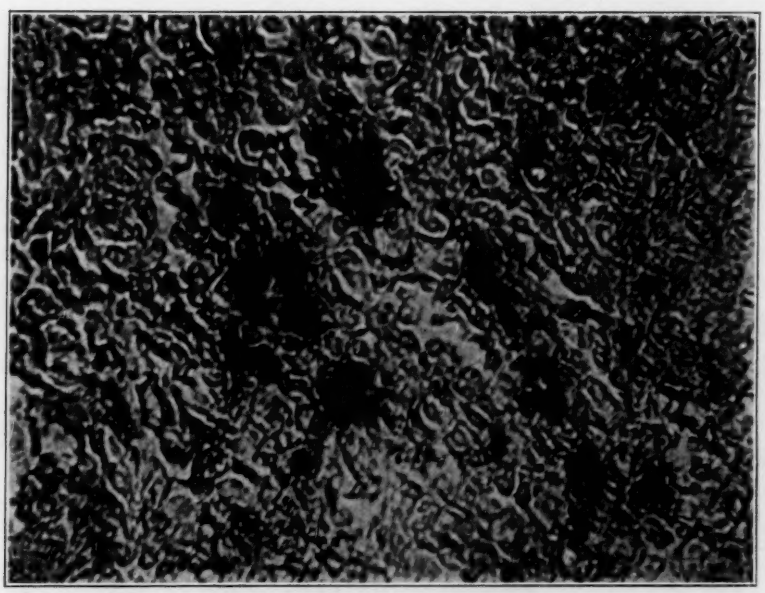

Fig. 4.—Same section as that in figure 3; × 720.

the hemoglobin iron remains fairly constant after the first day of life, but that there is a sharp drop followed by a rapid increase in the nonhemoglobin iron. In a rabbit of 3 days the nonhemoglobin iron exceeds the hemoglobin iron by 68 per cent. At 6 days this excess has reached 185 per cent. One may question the validity of applying to human beings quantitative data derived from rabbits. Nevertheless, our own histologic studies, the metabolic studies of Langstein and Edelstein and the studies on the blood made by Williamson indicate that the changes occurring during the first three months of human life are comparable to the changes that occur during the first six days of postnatal life in

21. Langstein and Edelstein: Verhandl. d. XXX Versamml. d. Gesellsch. f. Kinderh., 1913, p. 3.

the rabbit, namely, a doubling of the body weight, a moderate increase in total hemoglobin, a marked decrease in the percentage of hemoglobin and an early loss of iron followed by a progressive increase of hemoglobin iron but more particularly of nonhemoglobin iron.

SUMMARY

A series of livers obtained at autopsies on fetuses and infants was studied microscopically and chemically to determine the variations in the amount of iron present and the factors on which such variations depend.

There is no evidence microscopically or chemically of large or progressive depositions of iron in the liver during the last four months of intra-uterine life. Exclusive of iron as hemoglobin, the entire liver of the mature new-born infant contains on the average about 32 mg. of iron. Largest amounts of iron are found in the liver from one to ten weeks after birth, and these are believed to depend on postnatal intravascular destruction of blood.

Hemosiderosis of the liver may also result from hemorrhages into the tissues or cavities of the body of the fetus or infant, and during fetal life it may result from similar hemorrhages in the mother, the liberated iron reaching the fetal liver via the placenta.

Hemosiderosis of the spleen and the liver follows transfusions of blood, and the amount of iron found in the liver is influenced by the size and frequency of the transfusions. The appropriation and utilization of transfused blood are discussed.

It appears that the changes occurring during the first three months of human life are comparable to the changes that occur during the first six days of postnatal life in the rabbit, namely, a doubling of the body weight, a moderate increase in the total hemoglobin, a marked decrease in the percentage of hemoglobin and an early loss of iron followed by a progressive increase of hemoglobin iron but more particularly of nonhemoglobin iron.

The chemical analyses were made in the Chemistry Laboratory of the Babies' Hospital by Dr. Sullivan and her assistants. The livers studied were obtained from the departments of pathology of the Babies' Hospital, Sloane Hospital, Lying-In Hospital and Presbyterian Hospital.

SIMPLIFIED FEEDING TECHNIC FOR THE SMALL, PREMATURELY BORN INFANT

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The prematurely born infant, too young to suck and swallow, requires a special feeding technic. Catheter feeding (gavage), introduced by French physicians many years ago, has been the method of choice for infants weighing less than 4 or 5 pounds (1,814 or 2,267 Gm.). Some of the nurses who are skilled in the art of feeding by gavage consider nasal gavage less hazardous, but the catheter used must be small in diameter (6 to 10 F). The use of such a catheter may make the introduction of an ounce of food a tedious procedure. Such catheters are cleaned with difficulty, and curds of coagulated milk often obstruct the lumen. The mechanical irritation caused by the repeated introduction and extraction of the tube also detracts from this method of feeding of the smallest infants. Many graduate nurses have never used gavage for a prematurely born infant, and pupil nurses usually hesitate or manifest fear when passing the tube. Their main concern is the danger of entering the trachea. If the tube is passed beyond the cardia it not infrequently causes vomiting of food which has already entered the stomach. Feeding by gavage requires skill, judgment and courage.

The extreme smallness of such an infant makes it imperative that food be given without delay. The limited capacity of the stomach requires that the caloric value of the food be high. Because of the scant secretion of digestive juices, the food must be readily digestible. Since the tolerance of such an infant is limited, the food must be sterile and not readily fermentable. The feeding interval should be long because of the low motility of the stomach (emptying time). A feeding should not be very time-consuming. The reflex center for swallowing, which is located in the medulla, is not sufficiently developed, and the muscles of swallowing are still too feeble to function. Added to these difficulties are the listlessness of such infants, the instability of body temperature and the tendency to vomiting, diarrhea and loss of weight. The mechanical introduction of the proper food at regular intervals by

means of the catheter permits digestion, assimilation, gain in weight and growth. Gavage in the case of infants too small to suck and swallow has saved many lives.

During the past few years I have not used feeding by gavage for this type of infant. Twelve prematurely born infants weighing less than 4.5 pounds (2,040 Gm.) have been fed by a technic that has been evolved from Dr. Herbert Pott's method of feeding children with cleft palates after operation. It has proved so satisfactory that I have used it in place of gavage. It is continued until the infant has gained sufficient strength to take the Breck feeder or the bottle or to nurse at the breast.

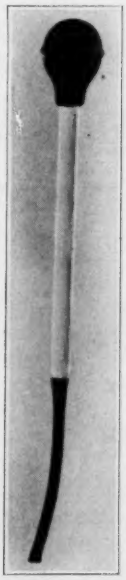

Fig. 1.—Pipet for feeding prematurely born infants.

TECHNIC

To the lower end of a long dropper or eye pipet is attached a piece of soft rubber tubing 8 cm. (3 inches) long and 5 mm. (⅛ inch) in diameter (wall, 1 mm.; lumen, 3 mm.). The outfit is sterilized by boiling for five minutes. The attendant sits beside the crib, steadies the infant's head with the left hand, fills the pipet by suction with warm breast milk (from 40 to 60 drops), gently inserts the soft rubber tubing at the side of the infant's mouth, passes it back to the base of the tongue (about 2 inches [5 cm.] from the gum line) and gently presses on the bulb after the tip of the tube has reached the posterior wall of the throat. As a rule, the first feeding is given from four to six hours after birth and consists of a few drachms of sterile, diluted breast milk. This procedure is repeated at intervals of three or four hours. The quantity and quality are gradually increased so that in forty-eight hours most prematurely born infants are given seven or eight feedings of 1 ounce (28.3 Gm.) of sterile, pasteurized, undiluted breast milk every

twenty-four hours. If there is a tendency to diarrhea, the breast milk is boiled in a single boiler for five minutes, sterile water replacing the amount lost by evaporation. If this does not correct the diarrhea, calcium caseinate (1 or 2 tablespoonfuls) is added to the milk before it is boiled. This is gradually reduced as the child's tolerance improves.

Fluoroscopic examinations [1] and roentgenograms taken at the time of feeding show that the milk flows from the pharynx into the stomach without being swallowed. An ounce of milk can thus be given to an infant weighing 3 pounds (1,360 Gm.) in less than ten minutes. No infant has become cyanotic as the result of this method of feeding, nor has food been aspirated. None of the infants so fed failed to gain after the first week; indeed, more than half never lost weight. As the infant's weight approaches 5 pounds, it will be noted that the hunger impulse, sucking act and swallowing usually develop spontaneously, and from

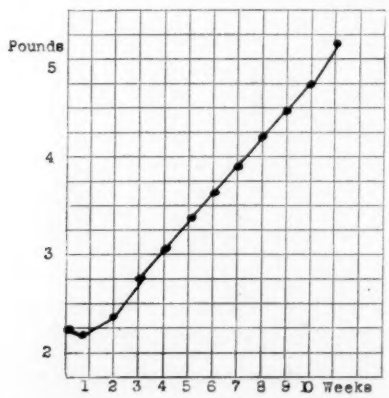

Fig. 2.—Chart showing gain in weight of Ellen W., eight weeks premature, who was fed exclusively by pipet.

then on, two and gradually more of the feedings may be given by Breck feeder or small nipple.

The smallest infant of 1930 fed exclusively by this technic was Ellen W., delivered by low cesarian section at the Evanston Hospital, on Sept. 12, 1930. At the time of delivery her condition was good; there were no injuries, and the cry was fairly good. Birth occurred sixty days before the computed time; the weight was 2 pounds and 4 ounces (1,020.5 Gm.). The previously outlined technic was strictly

1. A synopsis of Dr. L. W. Harwood's report follows: "This premature infant 1 week old, weighing about 4 pounds, was fed under the fluoroscope by a special feeding dropper. It was repeatedly noted that the breast milk (containing sterile barium sulphate) ran without interruption from the end of the dropper down the esophagus into the stomach. At no time could a swallowing action be noted. It was just a continuous stream from the end of the dropper down the esophagus into the stomach."

adhered to; on the fifth day the weight was 2 pounds and 3 ounces (992.2 Gm.), and from then on increased as shown in the weight chart. The child left the hospital at the age of 2 months, weighing 4 pounds and 12 ounces (2.154.5 Gm.). At this time four of the feedings were given by bottle and three by the rubber-tipped pipet. There was an initial loss of weight of 1 ounce (28.3 Gm.) and a gain of 41 ounces (1,162.33 Gm.) in fifty-seven days of pipet feeding. In 1931, the smallest infant up to the time this article was written weighed 3.25 pounds (1,474.2 Gm.). In no instance has increase in weight been less than 4 ounces (113.4 Gm.) a week; nor has there been difficulty in giving the food.

All nurses who have used the technic find it much simpler, more time-saving and safer than feeding by gavage. Dexterity and a little practice will enable any mother or nurse to feed an infant weighing 2, 3 or 4 pounds without gavage. This method possesses all of the advantages of tube feeding without any of the handicaps.

SOME ASPECTS OF THE CIRCULATION IN THE PREMATURE INFANT

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CHICAGO

I. BLOOD PRESSURE

The literature concerning the blood pressure values in premature infants is indefinite. Abt and Feingold,[1] in a recent review, stated that the systolic pressure in premature infants is low "depending on the length of gestation." Dioxades [2] claimed that the systolic pressure in premature infants is less than normal up to the time they reach puberty. Lesne and Binet [3] found the hypotension in their premature infants so marked that they could not determine the pressures. P. Balard [4] was able to read the pressure by means of the Pachon oscillometer in infants weighing from 1,330 to 1,500 Gm., and he succeeded in doing so in an infant weighing 950 Gm. However, he did not publish his results.

It is difficult to make any comparisons of the blood pressure values obtained by other authors, because different methods have been used to record them. However, for comparative purposes, a brief review of the results obtained by some who have studied the blood pressure in full term infants is presented. The results, grouped according to age, are as follows, 1 day: from 36.5 to 56.3 mm., Balard; [5] 55 systolic and 35 diastolic, Balard; [6] 43, Seitz and Becker [7] and Reis and Chaloupka; [8]

Aided by the Emil and Fanny Wedeles Fund of the Michael Reese Hospital for the Study of Diseases of the Heart and Circulation.

From the Premature Station of Sarah Morris Children's Hospital, and the Heart Station and X-Ray Laboratories of Michael Reese Hospital.

1. Abt, A. F., and Feingold, B. F.: Blood Pressure in Infancy and in Childhood, Am. J. Dis. Child. **40**:1285 (Dec.) 1930.

2. Dioxades, L.: Fetalismus des Kardiovasculärensystem, Ztschr. f. klin. Med. **108**:321, 1928.

3. Lesne, E., and Binet, L.: Recherches sur la circulation du nourrisson, Arch. de méd. d. enf. **23**:69, 1920.

4. Balard, P.: La tension artérielle et l'oscillometrie chez le nouveau-né, Nourrisson **9**:304, 1921.

5. Balard, P.: Modification, évolution du pouls et de la tension artérielle chez le nouveau-né dans les premier jours de la vie, étudié par l'oscillométrie, Compt. rend. Soc. de biol. **73**:483, 1912.

6. Balard, P.: Le pouls et la tension artérielle de l'enfant et du nouveau-né, Gaz. d. hôp. **86**:837, 1913.

7. Seitz, A., and Becker, F.: Ueber den Blutdruck beim Neugeborenen, Zentralbl. f. Gynäk. **44**:1338, 1924.

8. Reis, R. A., and Chaloupka, A. J.: Blood Pressure in the Newborn, Following Normal and Pathological Labor, Surg., Gynec. & Obst. **37**:206, 1923.

55 systolic and 40 diastolic, Rucker and Connell,[9] and 60.6, Ikeda;[10] 10 days: 70, Seitz and Becker;[7] 64 systolic and 41 diastolic, Rucker and Connell,[9] and 78, Reis and Chaloupka;[8] 1 month: from 64 to 68 systolic and 48 to 50 diastolic, Leitao;[11] 80, Seitz and Becker,[7] and 60, Lesne and Binet;[3] from 2 to 3 months: from 66 to 74 systolic and 48 to 56 diastolic, Leitao;[11] and 80, Lesne and Binet;[3] from 3 to 4 months: from 68 to 80 systolic and 48 to 50 diastolic, Leitao,[11] and 90, Lesne and Binet;[3] from 5 to 6 months, 100, Lesne and Binet.[3] Thus it can be seen that the figures in the literature vary considerably, and that the systolic pressure averages from 36.5 to 55 mm. the first day of life, and thereafter from 64 to 100 mm. in the first half year of life. The systolic pressures, taken by the method used in this work, of twenty-three full term infants from 1 day to 2 weeks of age fell in the foregoing range. The values varied from 58 to 88 mm.

METHOD

The blood pressure studies reported in this section were carried out on 78 premature infants; 34 were boys and 44 girls. There were 10 Negroes in the group.

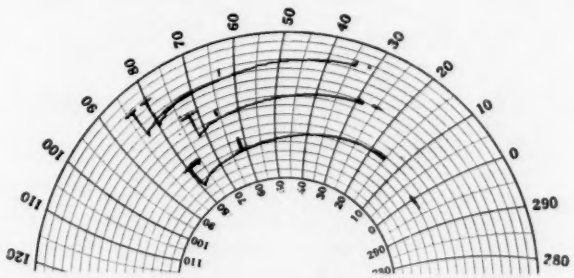

Fig. 1.—Typical blood pressure record. The systolic pressure averages 63 mm. Note that the observer's marks coincide with the first upstroke of the pen.

In all, 1,026 systolic readings were taken, the average of 3 readings being used each time for the final result. The averages are thus based on 342 determinations of the systolic pressure. The periods of gestation in these infants varied from six and a half to nine months. The weights of the infants, when the readings were first obtained, varied from 1,050 to 2,500 Gm.

A Tycos recording sphygmomanometer, which was loaned by the Taylor Instrument Companies, was used for the readings. This instrument was found to be sensitive enough, and at the same time reduced the personal element to a minimum. Since in the early readings the first pulsations that came through were not recorded, it was necessary to mark on the charts the points at which the first pulsations were seen. Occasionally, in the small and feeble infants,

9. Rucker, M. P., and Connell, J. W.: Blood Pressure in the New-Born, Am. J. Dis. Child. **27**:6 (Jan.) 1924.

10. Ikeda, K.: Physiologic Blood Pressure in Infants, J. Pediat. (Tokyo), September, 1925, p. 197; abstr., Am. J. Dis. Child. **33**:163 (Jan.) 1927.

11. Leitao, M.: Pression artérielle chez l'enfant, Arch. de méd. d. enf. **16**:102, 1913.

it was necessary to keep the pen above the chart to enable the observers to see the pulsations. At these times two observers recorded their readings separately. As the oscillations became more marked, it was found that the observer's marks and the first recorded upstrokes practically always coincided. The downstrokes of the pen, which are seen in readings on older persons and which are caused by the "hydraulic ram" effect, were not observed in the premature infants. About fifty satisfactory diastolic readings were obtained from the charts, and as many pulse pressures were computed (figs. 1 and 2 are examples of two of our typical records).

The measurements of the two rubber bags used were as follows: The upper bag measured 5 cm. in width and 15 cm. in length; the lower bag measured 6.5 cm. in width and 15 cm. in length. In order to avoid possible transfer of skin infections, a thin muslin cloth was wrapped around the extremity before the cuff was applied. This procedure caused no difference in readings, as was shown by tests. A bandage was wrapped around the cuff to insure a snug application.

It was decided to take the blood pressure readings on the lower extremity, because of several advantages: (1) There was a minimum of exposure of the infants; (2) the subject was least disturbed, and (3) the cuff could be much more snugly applied. Hoebler, as quoted by Rucker and Connell,[9] found thigh readings to be from 10 to 15 mm. higher than radial readings. Norris, Bazett and

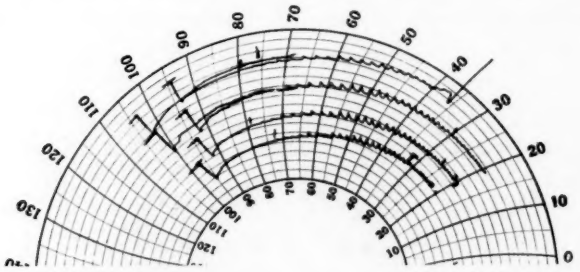

Fig. 2.—Typical blood pressure record. The systolic pressure averages 77 mm.; the diastolic, 29 mm.

McMillan,[12] however, stated that the systolic pressures in the arm and the leg of a person lying quietly in a horizontal position are equal. Our figures in nine comparative readings seem to agree with the latter statement. Reference to table 1 will show that five readings are practically alike; in three readings, the pressure in the thigh is from 8 to 13 mm. higher than that in the arm, while in the last one, the arm reading is 14 mm. higher than the thigh reading.

The first readings, when possible, were taken on the day of birth. They were then taken at weekly intervals as long as the patients were in the hospital, and then at approximately monthly intervals. Although the large majority of readings were taken on infants who were awake and quiet, the infants had to be fed in a few instances before readings could be obtained. The effect of the act of feeding on blood pressure will be discussed later.

RESULTS

Normal Blood Pressure in the Premature Infant.—Analysis of the data obtained presented some difficulty. The important factors on which

12. Norris, G. W.; Bazett, H. C., and McMillan, T. M.: Blood Pressure: Its Clinical Application, Philadelphia, Lea & Febiger, 1927, p. 111.

the blood pressure depended seemed to be weight and age. As the work proceeded, it became apparent that in grouping the pressures the more important factor was weight (see table 2). The dependence of blood pressure on body weight is in accord with the findings of Leitao [11] and Ikeda [10] on full term infants. Average blood pressure values were therefore obtained by grouping the figures according to weight.

Analysis of the figures in table 2 shows that the age factor apparently plays an important part, mainly in the first days of life, although there

TABLE 1.—*Arm and Thigh Readings (Systolic Pressures)*

Arm, mm. Hg.....	74	58/34	54	71	62	73/35	59/38	57	52
Thigh, mm. Hg.....	77	71/35	62	73	61	70/40	62/31	43	65

TABLE 2.—*Systolic Pressures Grouped According to Weight and Age*

	Age										
Weight, Gm.	1 Day	2 Days to 1 Wk.	1 Wk. to 2 Wk.	2 Wk. to 3 Wk.	3 Wk. to 4 Wk.	1 Mo. to 2 Mo.	2 Mo. to 3 Mo.	3 Mo. to 4 Mo.	4 Mo. to 5 Mo.	5 Mo. to 6 Mo.	6 Mo. to 7 Mo.
1,050 to 1,100.....	....	47.5	....	....	....	....	....	....	....	....	....
1,100 to 1,200.....	....	36.0	56.0	....	....	....	....	....	....	....	....
1,200 to 1,300.....	20.25	43.5	50.0	....	50.0	48.0	....	....	....	....	....
1,300 to 1,400.....	46.0	43.0	....	....	58.0	....	....	....	....	....	....
1,400 to 1,500.....	38.0	42.0	45.0	47.5	57.5	41.0	....	....	....	....	....
1,500 to 1,600.....	27.5	49.0	53.0	....	55.5	62.0	....	....	....	....	....
1,600 to 1,700.....	51.0	48.5	58.0	64.0	....	63.5	61.0	....	....	....	....
1,700 to 1,800.....	....	49.0	57.0	58.0	44.0	65.0	....	....	....	....	....
1,800 to 1,900.....	44.0	58.0	61.5	59.0	67.5	64.0	52.0	....	....	....	....
1,900 to 2,000.....	53.0	60.0	53.0	59.0	66.0	65.0	....	....	....	....	....
2,000 to 2,200.....	52.0	55.0	66.0	65.0	66.0	68.0	72.0	....	....	....	....
2,200 to 2,500.....	50.0	69.0	59.0	65.0	71.0	70.0	79.0	....	....	....	....
2,500 to 2,750.....	....	....	68.0	....	75.0	72.0	77.5	....	....	....	....
2,750 to 3,000.....	....	....	....	....	....	75.0	72.5	....	....	....	....
3,000 to 3,250.....	....	....	....	....	....	72.0	79.0	....	....	....	....
3,250 to 3,500.....	....	....	....	....	....	86.5	84.0	90.0	....	....	....
3,500 to 3,750.....	....	....	....	....	....	....	81.0	81.0	....	....	....
3,750 to 4,000.....	....	....	....	....	....	71.0	77.0	....	....	....	....
4,000 to 4,250.....	....	....	....	....	....	....	85.0	....	....	....	....
4,250 to 4,500.....	....	....	....	....	....	....	75.0	86.0	....	....	....
4,500 to 4,750.....	....	....	....	....	....	....	107.0	82.0	....	....	....
4,750 to 5,000.....	....	....	....	....	....	....	....	....	....	....	....
5,000 to 5,250.....	....	....	....	....	....	....	87.0	....	....	....	....
5,250 to 5,500.....	....	....	....	....	....	....	87.0	....	....	....	....
5,500 to 5,750.....	....	....	....	....	....	....	....	....	72.5	90.0	....
5,750 to 6,000.....	....	....	....	....	....	....	....	....	97.0	95.0	....
6,500 to 6,750.....	....	....	....	....	....	....	....	....	....	....	93.0
7,000 to 7,250.....	....	....	....	....	....	....	....	....	....	89.0	....

is a tendency, on the whole, for older infants of a certain weight to have higher pressures than younger infants of the same weight. The systolic pressure seems to be lower the first day of life than on the days immediately following, regardless of weight; similarly, it tends to be lower the first week of life than during the second week and later. The systolic pressure readings for the first day fluctuate somewhat widely between 20.25 and 50 mm. for infants weighing less than 1,900 Gm., with one exception of 51 mm. The average systolic pressure on the day of birth for infants weighing over 1,900 Gm. is 50.53 mm.

The figures for systolic pressure in table 4 show that while the readings during the first week of life are lower than those during the following weeks, there is a tendency for the pressure to increase during this age period with a gain in weight. The average systolic pressures

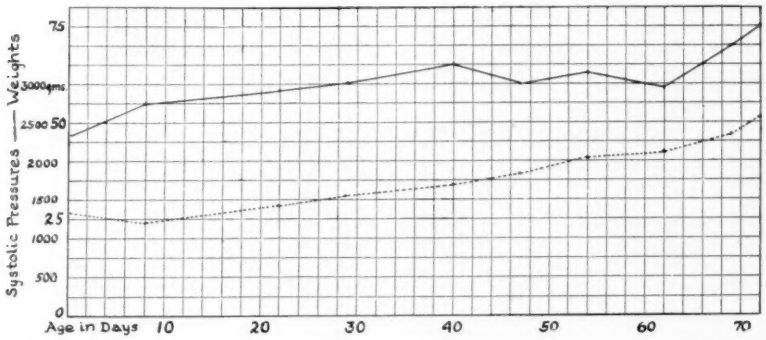

Fig. 3 (Girl G.).—The first pressure was taken when the infant was 1½ hours old; she weighed 1,280 Gm. The solid line represents the pressure; the broken line, the weight.

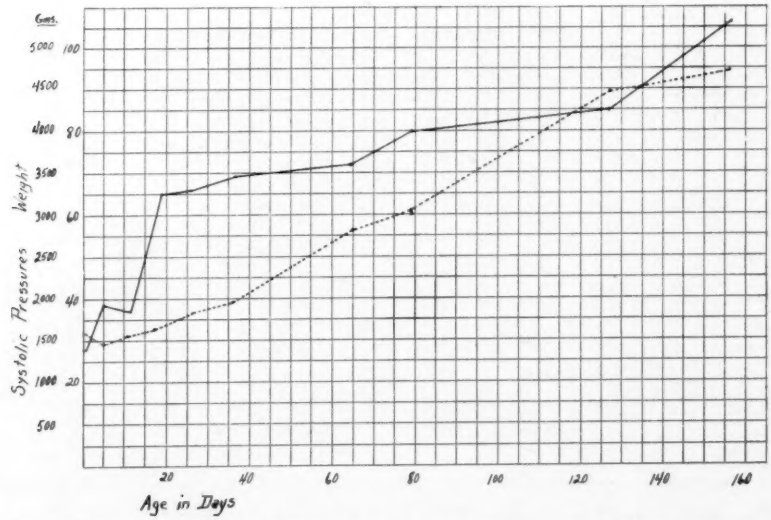

Fig. 4 (Baby B.).—The first reading was taken when the infant was 4 hours old; the weight was 1,525 Gm. The solid line represents the pressure; the broken line, the weight.

in infants older than 1 week in the group between 1,100 and 1,600 Gm. vary between 50 and 57 mm. The pressure in infants weighing more than 1,600 Gm. shows a steady increase until a weight of 3,500 Gm. is reached. Above 3,500 Gm., no correlation between weight and systolic

pressure can be made. The systolic pressure then averages between 80 and 95 mm.; with one low average of 75 mm.

A study of the variation in systolic pressure in two of our typical infants (figs. 3 and 4) shows that the pressure and weight curves are

TABLE 3.—*Diastolic Pressures Grouped According to Weight*

Weight, Gm.	Diastolic Pressures	Average
1,500 to 1,600	26, 26	26.0
1,700 to 1,800	27.5	27.5
1,800 to 1,900	34, 21	27.5
1,900 to 2,000	39	39.0
2,000 to 2,100	30, 45, 34, 25, 37, 30, 35, 32, 38	34.0
2,100 to 2,200	40, 30, 35, 37, 30	34.0
2,200 to 2,300	35, 42, 32, 35, 27	34.0
2,300 to 2,400	34	34.0
2,400 to 2,500	38, 30	34.0
2,500 to 2,750	24, 27, 35, 36, 41, 42, 37, 38	35.0
2,750 to 3,000	27, 27.5	27.0
3,000 to 3,250	29, 37	33.0
3,500 to 4,000	37, 32.5, 30	33.2
4,000 to 4,250	41.5	41.5
4,250 to 4,500	42	42.0
4,500 to 4,750	38	38.0
4,750 to 5,000	46	46.0
5,000 to 5,250	30, 45, 36.5	37.1
5,250 to 5,500	30	30.0
5,500 to 5,750	38	38.0
5,750 to 6,000	38	38.0
6,000 to 6,500	41	41.0
7,000 to 7,500	42	42.0

TABLE 4.—*Average Systolic Pressures, Diastolic Pressures and Pulse Pressures*

Weight, Gm.	Systolic Pressure, 2 Days-1 Week	Systolic Pressure	Diastolic Pressure	Pulse Pressure
1,000 to 1,100	47.5	....	....	....
1,100 to 1,200	36.0	56.0	....	....
1,200 to 1,300	43.5	50.0	....	....
1,300 to 1,400	43.0	58.0	....	....
1,400 to 1,500	42.0	47.0	....	....
1,500 to 1,600	49.0	57.0	26.0	31.0
1,600 to 1,700	48.0	59.0	....	....
1,700 to 1,800	49.0	59.0	27.5	31.5
1,800 to 1,900	56.0	61.0	27.5	33.5
1,900 to 2,000	61.0	62.0	39.0	23.0
2,000 to 2,200	55.0	66.0	32.0	34.0
2,200 to 2,500	69.0	71.0	34.0	37.0
2,500 to 2,750	....	71.0	35.0	36.0
2,750 to 3,000	....	73.0	27.0	46.0
3,000 to 3,250	....	75.0	33.0	42.0
3,250 to 3,500	....	86.0	....	....
3,500 to 3,750	....	80.0 }	33.2	44.3
3,750 to 4,000	....	75.0 }		
4,000 to 4,250	....	85.0	41.5	43.5
4,250 to 4,750	....	90.0	46.0	44.0
4,750 to 5,000	....	93.0	37.0	56.0
5,000 to 5,500	....	87.0	35.0	52.0
5,500 to 5,750	....	80.0	38.0	42.0
5,750 to 6,000	....	97.0	38.0	59.0
6,000 to 6,250	....	95.0	41.0	54.0
6,250 to 6,500	....	....	....	....
6,500 to 7,000	....	93.0	....	....
7,000 to 7,250	....	89.0	42.0	47.0

roughly parallel in the individual case. However, the age factor is of some importance, since the curve of Baby B's (fig. 4) systolic pressure shows a rise in pressure during the first week, while there is an initial weight loss.

The lowest systolic pressure obtained was 20.25 mm. of mercury in an infant weighing 1,225 Gm. This patient died on the day of birth. All the other low readings, which were taken within the first twenty-four hours of life of infants who lived, were as follows: (1) weight 1,480 Gm., pressure 27 mm.; (2) weight 1,590 Gm., pressure 27.5 mm.; (3) weight 1,575 Gm., pressure 28 mm.; (4) weight 1,860 Gm., pressure 31 mm.; (5) weight 1,455 Gm., pressure 35 mm.; (6) weight 2,010 Gm., pressure 38 mm.

Since we accepted only fifty-six diastolic readings as being probably correct, no attempt was made to analyze the figures according to age, the pressures being grouped according to the weights of the infants. The results and the averages are tabulated in table 3. Analysis of these figures shows that the diastolic pressure does not change much, although it increases slightly with an increase in weight. The average figures range from 26 to 46 mm. They can be roughly grouped as follows: from 1,500 to 1,900 Gm., the diastolic pressure fluctuates between 26 and 27.5 mm. with occasional higher readings; from 1,900 to 4,000 Gm., the diastolic pressure averages approximately from 33 to 39 mm., and from 4,000 to 6,000 Gm., the diastolic pressure averages between 37 and 46 mm. The average pulse pressure also goes up, with occasional fluctuations, as the weight increases (table 4). This, of course, would be expected in view of the fact that the diastolic pressure increases little as compared with the rise of the systolic pressure.

When one compares the results herein tabulated with the figures given for full term infants, it is apparent that premature infants weighing less than 2,000 Gm. have lower systolic pressures during the first days of life and later than those of full term infants of the same postnatal age. Premature infants weighing over 2,000 Gm. have approximately the same and even higher systolic pressures than some of the values given by other authors for full term infants. The diastolic pressures obtained in this study, however, all seem to be lower than those given by other authors for full term infants.

The Effect of Some Normal Factors on Blood Pressure.—As far as possible other factors that might influence the blood pressures have been analyzed. In such analyses the systolic pressures were grouped according to body weight and compared.

The following factors, on analysis, seem to have no definite effect on the systolic blood pressure, i. e., degree of prematurity, body length, race, thigh and leg circumference, body temperature and time of day the reading was made.

There is a tendency for the females to have somewhat higher systolic pressures than the males, the difference being from 1.5 to 6 mm. of

mercury. In considering this factor, only those averages were considered in which fair numbers of observations in each sex could be compared.

On twenty occasions it was necessary to resort to feeding the infants in order to keep them quiet while the readings were taken. If one waited for a few minutes until the first vigorous suckling was over, the systolic pressure came down to a constant level, lower than when the feeding began. Eight of these stabilized readings were from 7 to 15 mm. higher than the averages for the weight; two were less than the average, and ten were within the average range.[13]

TABLE 5.—*The Relation of Maternal Prepartum Hypertension to Systolic Pressure*

Sex	Name	Weight, Gm.	Age	Systolic Pressure	Average Systolic Pressure for Weight	Mother's Blood Pressure
Girl	C.	1,220	14 hours	31.0	No average	175/110
Girl	D.	2,020	12 hours	55.0	52	180/114
Girl	H.	1,745	4½ hours	50.0	49	200/130
Girl	H.	1,805	12 days	54.0	60	200/130
Girl	H.	1,900	19 days	67.0	62	200/130
Girl	K.	1,900	13 hours	58.0	53	160/100
Girl	L_1	1,515	5 days	70.0	49	130/ ? *
Girl	L_2	1,755	5 days	59.0	49	170/ ?
Girl	L_2	1,875	12 days	59.0	61	170/ ?
Girl	S_1	1,688	4½ hours	61.0	51	158/ 90
Girl	S_1	1,675	9 days	75.0	59	158/ 90
Girl	S_1	1,830	17 days	71.5	60	158/ 90
Girl	S_1	2,000	26 days	66.0	66	158/ 90
Boy	S_2	1,480	3⅜ hours	27.0	38	170/130
Boy	S_2	1,360	4 days	41.0	43	170/130
Boy	S_2	1,400	11 days	63.0	47	170/130
Boy	S_2	1,405	12 days	79.0	47	170/130
Boy	S_2	1,460	18 days	66.0	47	170/130
Boy	S_2	1,570	27 days	59.0	57	170/130
Boy	S_2	1,745	34 days	67.0	61	170/130
Boy	V.	2,235	24 hours	45.0	52	148/ 90
Boy	V.	2,140	7 days	62.0	55	148/ 90
Boy	V.	2,150	14 days	55.0	66	148/ 90
Boy	V.	2,240	19 days	63.0	71	148/ 90

* Mild toxemia.

In twenty-seven observations on sleeping infants, twelve readings showed a definite lowering of the systolic pressure of from 8 to 46 mm. below the average figures for these weights. Three readings were definitely higher than the average figures, and twelve were within average range. These results are different from the observations on full term infants, in whom a fall in systolic pressure always occurs during sleep.

Twenty readings were taken in infants just after they had stopped crying. In eight of these observations, the systolic pressures were increased from 6 to 23 mm. above the average for the weights; in one

13. The effect of feeding, sleeping and crying is similar in individual cases when the readings are compared with the curve of the rise in blood pressure with the age and weight of the infant.

the reading was below average, and in eleven the results were within the average range. Moving was also found to cause an increase in systolic pressure, but there were not enough readings to give average figures.

The Effect of Some Abnormal Factors on Blood Pressure.—We were able to make observations on nine infants whose mothers had definite hypertension on the day the infants were born. Two of the nine infants died on the day of birth. The weights of these infants, their systolic pressures, the average systolic pressure for premature infants for their weights and the blood pressures of their mothers are shown in table 5. Five had systolic pressures within the average range. The reading on Baby L_1 was a systolic pressure of 70 mm., as compared with the average for its weight of 49 mm. The first reading on Baby

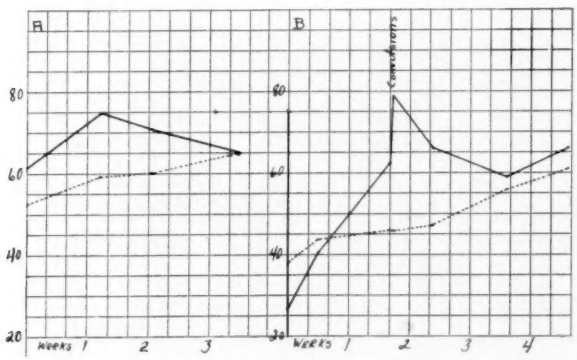

Fig. 5 (Baby S_1 [*A*] and Boy S_2 [*B*]).—The mothers of these two infants had hypertension. The upper curves represent the readings on the patient; the lower curves, the average.

L_2 was 10 mm. higher than average for his weight. The second one taken at the end of twelve days had returned to the average. Baby S_1 (fig. 5 *A*) showed a pressure above the average from the first day of life. At the end of seventeen days the pressure was still above average, but it had dropped to the average at the age of 26 days.

Baby S_2 (fig. 5 *B*) presented an interesting case. The mother's prepartum blood pressure was 170 systolic and 130 diastolic. The systolic pressure obtained on the first and fourth days of the life of the infant was within the average range. However, on the eleventh day his systolic pressure was 16 mm. above the average figure for his weight. The following day the infant began to show twitchings and convulsions. Following these convulsions the systolic pressure rose to 103 mm., or two and one-half times the average figure, but it fell in a few minutes

to a constant level of 79 mm. The last reading, taken when the infant was 34 days old, was still slightly elevated, although probably within the average range. Spinal puncture performed the day the patient had the convulsions gave a bloody spinal fluid. Whether the convulsions were due to a toxic condition of the infant or to a fresh intracranial hemorrhage cannot definitely be stated.

In addition to the increased systolic pressures observed in four infants of the preceding group, we observed a case of hypertension in a premature infant (fig. 6) whose period of gestation was nine and one-half lunar months, and whose birth weight was 2,330 Gm. From the first day of life this infant had a high systolic pressure which ran from

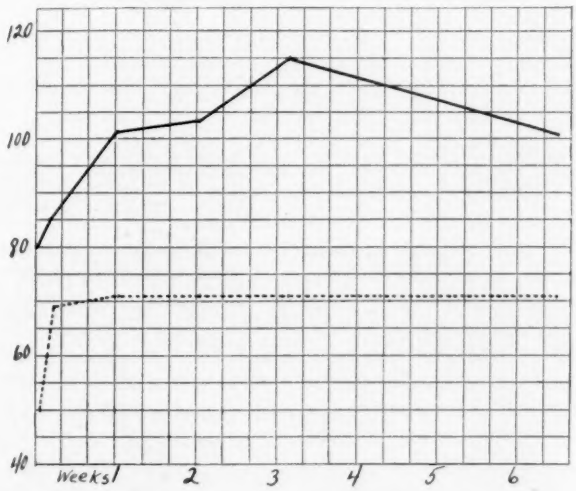

Fig. 6 (Baby A.).—The upper curve represents the readings on the patient; the lower curve, the average.

15 to 45 mm. higher than the average, the systolic pressure at the age of 8½ hours being 80 mm. The last systolic pressure, taken at the age of 46 days, when the weight was 2,435 Gm., was 103 mm. At the age of 15 days, the systolic pressure taken soon after the infant had moved and cried was 142 mm.; it fell in two minutes to 110 mm. The satisfactory diastolic readings obtained at the age of 8 and 23 days were 55 and 60 mm. respectively. The patient's weight increased only 200 Gm. during these observations. This patient returned to the hospital with bronchopneumonia, and died at the age of 58 days. At autopsy, there were no unusual changes in the heart. The kidneys were normal. No arterial changes could be noted. It should be mentioned that the mother's blood pressure was 110 systolic and 76 diastolic.

Of the infants studied in this work, five died within the first few days after their admission. Their systolic pressures and the autopsy observations are shown in table 6.

With the exception of Baby H., who had the lowest reading obtained, the pressures were not low as compared with the first day pressures on infants who survived. It is of interest to note that one of these infants

TABLE 6.—*Systolic Pressures in Infants Who Died*

Name	Age	Weight, Gm.	Systolic Pressure	Average Pressure	Autopsy Observations	Comment
T.	9 hr.	1,485	48	Other readings in first 24 hours in those who lived, 27, 43 and 43	Almost absent interventricular septum; supracortical, subarachnoidal hemorrhage; atelectasis	Gestation 7½ mo.; congenital heart anomaly; pressure higher than in those of same weight who lived; died in first 24 hours
H_1	5½ hr.	1,225	20.25	None for comparison in this weight group; one weighing 1,070 Gm. had pressure of 48	Meningeal congestion; no intracranial hemorrhage	6½ months' gestation; died when 4 days old; had been having cyanotic spells
H_2	4 hr.	1,790	55	Average 44 (51, 50, 30.5)	Subdural, subtentorial and intraventricular hemorrhage; marked atelectasis	7½ months' gestation; hemorrhage around medulla; pressure here higher than average
C.	14 hr.	1,220	31	No readings for comparison	Subarachnoidal supracortical clot	Mother had hypertension
D.	12 hr.	2,020	55	52	No autopsy	Mother had hypertension; systolic pressure normal

TABLE 7.—*The Effect of Spinal Puncture on Systolic Pressure (Performed in All Cases Because of Cyanosis)*

Name	Amount and Type of Fluid	Pressure Before	Pressure After	Weight, Gm.
M.	2 cc. clear; xanthochromic	62	64.0	1,830
B_1	1.5 cc. clear; xanthochromic	53	44.0	1,590
F.	3 cc. clear; xanthochromic	31	40.0	1,095
B_2	2 cc. clear; xanthochromic	38	31.0	1,445
G.	10-15 cc.; blood-tinged	69	61.0	3,600
K.	2 cc. clear; xanthochromic	57	51.5	1,920
W.	1.5 cc. clear; xanthochromic	62	53.0	1,765

had a congenital heart anomaly which apparently did not affect the systolic pressure; in fact, the systolic reading was 5 mm. higher than the highest first day pressures in infants of his weight.

We were able to note the changes in systolic pressure produced by spinal puncture in seven instances. The readings were made about five minutes before, and five minutes after, the spinal punctures. The blood pressure cuff was left in place during the punctures to eliminate any error from that source. The results are shown in table 7. Just as has

been observed in adults (H. Kahler [14] and Block and Oppenheimer [15]), the systolic blood pressure in our premature infants showed a tendency to fall with the removal of spinal fluid. The pressure in five of the seven dropped from 5.5 to 9 mm. In one case, the systolic pressure was constant, while in another it rose 9 mm.

Since Balard [4] made the statement that the hypotension in premature infants, especially in those who are syphilitic, tends to persist, we thought it might be of interest to compare the pressures in the syphilitic infants in this group with the averages for their weights. With one exception these infants do not have a persistent low systolic pressure.

The factor of jaundice was not analyzed since practically all of the premature infants had jaundice that persisted over fairly long periods of time.

II. THE ELECTROCARDIOGRAM AND PULSE RATE

Several scattered studies of the electrocardiograms of premature infants have been made. Hecht,[16] in 1913, included a study on three premature infants in his article on the heart action in children. Seham [17] has included two premature infants in his paper on the electrocardiogram in normal children. Dioxades [2] discussed the form of the electrocardiogram in premature infants, and finally Burghard and Wunnerlich [18] (who mentioned Heubner and Noeggarth as having studied the electrocardiogram in premature infants) have included in their paper the electrocardiograms taken on thirty-two infants weighing less than 2,500 Gm. The findings of some of these authors and of other authors who observed the electrocardiogram in full term infants will be discussed in connection with our findings.

METHOD

The present study is based on the electrocardiograms taken on twenty-five premature infants who averaged 2,132 Gm. in weight when the first records were taken. The lightest infants in this group, three in number, weighed from 1,485 to 1,500 Gm.; the heaviest infant weighed 2,580 Gm. There were eleven boys and fourteen girls in this group, which included five Negro infants. The youngest infants studied were 2 days old when the first record was made. Records were obtained during the first twenty-four days of life in twenty infants. The remain-

14. Kahler, H.: Ueber das Verhalten des Blutdrucks nach der Lumbalpunktion bei Zerebralprozessen, Wien. klin. Wchnschr. **33**:1007, 1920.

15. Block, E. B., and Oppenheimer, R. H.: A Comparative Study of Intraspinal Pressure, Blood Pressure and Intra-Ocular Tension, Arch. Neurol. & Psychiat. **11**:444 (April) 1924.

16. Hecht, A. F.: Der Mechanismus der Herzaktion im Kindesalter, seine Physiologie und Pathologie, Ergebn. d. inn. Med. u. Kinderh. **11**:329, 1913.

17. Seham, Max: The Electrocardiogram in Normal Children, Am. J. Dis. Child. **21**:247 (March) 1921.

18. Burghard, E., and Wunnerlich, A.: Das Elektrokardiogram des Säuglings, des Neugeborenen und des Frühgeborenen, Ztschr. f. Kinderh. **45**:56, 1928.

ing five records were obtained during the second month of life. Follow-up records were obtained in sixteen of these infants, in some as late as the fifth or sixth months of life.

The first records were made with a mobile electrocardiograph, the infants lying in their incubators in the premature station while their electrocardiograms were taken. The follow-up records were taken in the Heart Station. At times it was necessary to allow the older infants to take feedings before the records were taken.

RESULTS

Amplitude and Form.—Analysis of the figures obtained revealed no relationship between electrocardiogram and weight changes, so that the results were arranged under several age groups. The data are shown in table form (table 8). Table 8 indicates the six groups into which the infants were divided for this study.

TABLE 8.—*Age Groups*

Group	Number of Infants in Group	Average Age	Average Weight, Gm.
1	9	4.2 days (2 to 7)	2,191 (1,500-2,500)
2	5	10.6 days (10 to 14)	1,879 (1,485-2,580)
3	5	20.6 days (17 to 24)	2,221 (1,870-2,460)
4	7	1 mo. 20 days (1 mo. 6 days to 2 mo. 4 days)	2,240 (1,990-2,825)
5	8	3 mo. 13 days (3 mo. 4 days to 3 mo. 21 days)	4,810 (3,905-6,000)
6	6	5 mo. 10 days (4 mo. 15 days to 5 mo. 26 days)	5,250 (4,760-6,580)

TABLE 9.—*Average Amplitudes P_1, P_2 and P_3*

Group	P_1	High	Low	P_2	High	Low	P_3	High	Low
1	0.9	1.3	0.4	0.9	1.3	0.3	0.2	0-1.1	0 to —0.8
2	0.7	1.0	0.4	1.3	1.7	0.9	0.9	1.4	0.5
3	0.7	1.2	0.3	0.9	1.1	0.6	0.35	0.6	—0.35
4	0.7	1.1	0.4	1.0	1.4	0.5	0.3	0.8	0
5	0.9	1.2	0.5	1.1	1.6	0.8	0.4	0 to 1	0 to —0.5
6	0.8	1.5	0.5	1.2	1.5	0.9	0.5	0.9	0

Seham [17] mentioned that the average height for P_1 in the first two years of life is 0.5 mm., and that the average height of P_2 in infancy is 1.2 mm.[19] He also found inverted or diphasic P waves in eight records, of which six were of new-born infants. Neither of his premature infants showed any P waves. Burghard and Wunnerlich [18] stated that the P waves are small.

Analysis of our figures (table 9) shows a tendency for the P wave in lead II to increase in amplitude as the infants grow older, while P_1 and P_3 change very little. P_2 is higher throughout than P_1 or P_3. P_3 (fig. 9 *B*) is usually rather low; it was absent four times and inverted five times (figs. 7*A*, 8 *B*, 9 *A* and 10). The absence of P_3

19. Whenever figures in literature are mentioned they were obtained on full term infants unless otherwise noted.

occurred in older infants only. The negative P_3's were observed in the earlier records, and tend to disappear in the later records in all but one case. The average amplitudes of P_1 observed by us are all higher than the figure mentioned by Seham for full term infants, while P_2 is of about the same height as that mentioned by him. P_1 and P_2 (figs. 7 and 8) frequently have peaked forms in the early records, this phenomenon being most marked in lead II. There is a tendency for P_1 and P_2 to flatten out as the infants grow older (figs. 8 *B* and 9 *B*), although in some instances the form persists.

All observers have found a right axis deviation in early infancy, both in full term infants and in premature infants. Smith [20] stated that

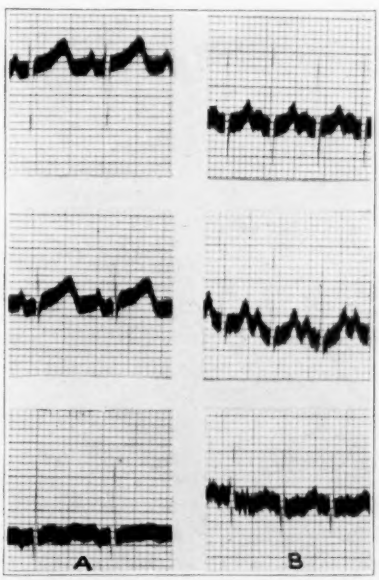

Fig. 7.—Electrocardiographic record; *A* was taken at the age of 7 days; *B*, at the age of 4 months and 28 days.

the right axis deviation tends to disappear about the fifth week, although this may vary. Krumbhaar and Jenks [21] found that the right axis shift disappeared in the second or third month, while Burghard and Wunnerlich [18] stated that this change occurs in the first quarter year.

In our series, the tendency to right axis deviation (figs. 7, 8 and 10) was also the rule during the first weeks of infancy (table 10). In all

20. Smith, S. C.: The Heart in Mothers and the New-Born, J. A. M. A. **79**:3 (July 1) 1922.

21. Krumbhaar, E. B., and Jenks, H. H.: Electrocardiographic Studies in Normal Infants and Children, Heart **6**:189, 1915.

but one case, Q R S was inverted in the earlier groups. During the second half of the first month and during the second month, about 35 per cent already showed a shift to an upright Q R S in lead I. In the older two groups, only two infants showed a persistence of the right axis deviation. The shift, therefore, occurred in our infants at from 1 to 3 months of age. In the first three groups there were two instances of left axis deviation, and three in which Q R S was upright in all leads.

In the following discussion amplitude of Q R S refers to the amplitude of the major deflection in the Q R S complex. The amplitude of

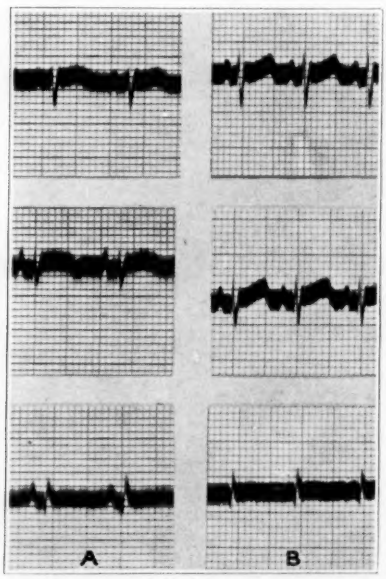

Fig. 8.—Electrocardiographic record; *A* was taken at the age of 12 days; *B*, at the age of 1 month and 10 days.

Q R S_3 was higher than that of Q R S_2 during the first two months of life, this difference decreasing as the infants grew older. During the third month, and from then on, the Q R S was tallest in lead II and next tallest in lead III. Q R S_1 (fig. 8 *B*) was diphasic (that is, it consisted of two phases of approximately the same height) five times. The diphasic Q R S_1 occurred mostly in the older groups. Q_2 and Q_3 tended to be deep, with Q_3 deeper than Q_2. This characteristic was more marked in the older infants of our series.

The level of the S-T segment in the electrocardiograms of infants was not mentioned in any of the papers we have read. Table 11 shows the distinct tendency for a high S-T_1 and S-T_2 in the early groups; S-T_3 throughout is iso-electric. The short high S-T take-off (figs. 7 *A*

and 9 *A*) tends to disappear in the older infants. Usually the short high take-off of the S-T in leads I and II is followed by a positive T.

Krumbhaar and Jenks [21] found the T wave to be absent in the first week of life. Seham [17] noted no T waves in the electrocardiagrams of his two premature infants, and stated that during the first ten days of life in full term infants he found T_1 present in 39 per cent, T_2 in 77

TABLE 10.—*Average Amplitudes of the Major Deflection in the Q R S Phase*

	Q R S_1			Q R S_2			Q R S_3		
Group	Average	High	Low	Average	High	Low	Average	High	Low
1	—7.8*	—2.2	—13.0	5.0	8.0	—2.7	8.2	14.0	5.2
2	—5.1	—3.0	—9.0	5.9	12.0	1.9	8.5	17.0	2.1
3	0.1	6.4	—5.6	3.8	13.0	—6.2	7.2†	11.6	4.5
4	0.1	6.3	—4.6	4.0	7.3	2.5	6.0‡	8.8	3.1
5	6.1§	8.0	2.5	13.1	22.0	4.1	9.6	17.0	2.5
6	7.3#	9.8	4.0	15.2	21.0	9.0	12.0	16.2	7.5

* Q R S_1 in one case was positive, with amplitude 6.
† Q R S_2 in one case was negative, with amplitude —9.
‡ Q R S_3 in one case was negative, with amplitude —3.
§ Q R S_1 in one case was negative, with amplitude —8.9.
# Q R S_1 in one case was negative, with amplitude —5.8.

TABLE 11.—*Average Levels of the S-T Segments*

	S-T_1			S-T_2			S-T_3		
Group	Average	High	Low	Average	High	Low	Average	High	Low
1	0.9	1.2	0	0.1	0.8	—0.4	0.1	0.4	0
2	0.7	1.0	0.5	0.7	1.1	0.4	0	0.2	0
3	0.1	0.1	0	0.1	0.3	0	0	0	0
4	0.25	0.8	0	0.2	1.0	0	0.1	0.8	0
5	0.3	1.0	0	0.2	0.5	0	0	0	0
6	0	0.2	0	0.1	0.5	0	0	0	0

TABLE 12.—*Average Amplitudes of the T Waves*

	T_1			T_2			T_3		
Group	Average	High	Low	Average	High	Low	Average	High	Low
1	1.2	2.2	0.4	0.7	2.0	0.4	—0.4	0.8	—0.9
2	1.2	2.0	0.8	1.4	2.5	0.9	0.6	1.4	0
3	1.2	1.8	0.7	1.4	2.0	0.3	0.1	4.5	—0.8
4	1.4	1.8	1.0	1.6	2.0	1.0	—0.1	0	—0.8
5	2.2	3.2	1.3	2.1	3.8	1.1	—0.4	0	—0.8
6	1.8	2.3	1.2	2.2	3.6	1.3	0	0.5	—0.6

per cent and T_3 in 47 per cent. Burghard and Wunnerlich [18] found T_3 to be negative. In our series T_1 and T_2 were present and distinct at all times (table 12). With two exceptions, T_2 was higher than T_1; T_3, however, was frequently absent or inverted (figs. 8 and 9 *B*), and when positive was low in amplitude. It was absent ten times and inverted nineteen times, the latter tendency being most marked in the younger infants. Follow-up records taken in some of the cases showing a negative T_3 revealed a persistence of this characteristic in two instances, a

disappearance of T_3 in three and a shift to a positive T_3 in two. Where T_3 was absent in the records of the younger infants, it stayed absent or became negative in the follow-up electrocardiograms. Two positive T_3's disappeared, and four positive T_3's became negative. Generally speaking, the T waves in the younger infants tended to be broad in appearance. This character tended to disappear in the older infants of our series. When Q R S_3 (fig. 9) was negative, T_3 was upright.

The amplitudes (fig. 8) of all the complexes, on the whole, tended to be low in the first three age groups. In the older groups they were relatively high, with a tendency, at times, for the low amplitudes to persist.

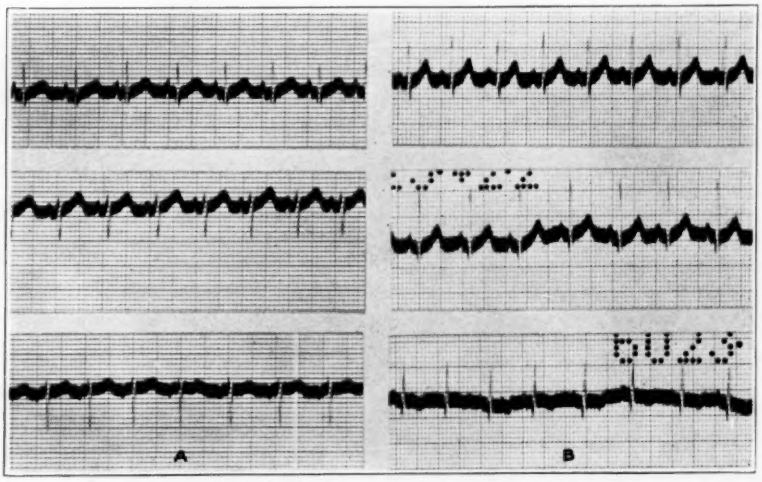

Fig. 9.—Electrocardiographic record; *A* was taken at the age of 21 days; *B*, at the age of 3 months and 13 days.

Duration.—We found no values in the literature for the duration of the P wave in infants. P_1 and P_2 tended to be about equal throughout (table 13). With some fluctuations, P_1 and P_2 increased in duration as the infants became older. The average duration of P_1 (excluding the average of 0.05 in group I) increased with age from 0.039 in group 2 to 0.058 second in the oldest group, and that of P_2 increased from 0.044 to 0.056 second. This change, of course, fits in with the tendency for P_1 and P_2 to lose their peaked forms as the infants became older. P_3 was frequently absent, and when present was of short duration; i. e., the average was 0.033 second, varying from a high average 0.042 second to a low of 0.023 second.

Seham [17] found the average duration of the P-R interval in newborn infants to be 0.113 second; in infants varying in age from 11 days to 1 year, the average was 0.125 second. Krumbhaar and Jenks [21]

observed the P-R interval to average from 0.08 to 0.12 second during the first week of life. In this series, P-R_1 and P-R_2 tended to be about equal and constant throughout (table 14). The averages varied from 0.095 to 0.106 second. P-R_3 was shorter throughout than the P-R interval in the two other leads, the average figures varying from 0.085 to 0.095 second. We noted no increase in P-R during the first six months of life in these infants.

TABLE 13.—*Average Durations of the P Wave*

	P_1			P_2			P_3		
Group	Average	High	Low	Average	High	Low	Average	High	Low
1	0.050	0.060	0.04	0.044	0.07	0.02	0.036	0.05	0
2	0.039	0.045	0.03	0.047	0.06	0.04	0.035	0.04	0.03
3	0.046	0.060	0.04	0.056	0.07	0.04	0.042	0.07	0.03
4	0.042	0.060	0.03	0.043	0.06	0.03	0.030	0.04	0
5	0.052	0.080	0.04	0.050	0.06	0.03	0.023	0.04	0
6	0.058	0.070	0.04	0.056	0.07	0.04	0.036	0.05	0.03

TABLE 14.—*Average Durations of P-R Interval*

	P-R_1			P-R_2			P-R_3		
Group	Average	High	Low	Average	High	Low	Average	High	Low
1	0.096	0.12	0.08	0.106	0.12	0.09	0.085	0.12	0.06
2	0.102	0.13	0.08	0.102	0.12	0.08	0.096	0.12	0.08
3	0.102	0.12	0.09	0.098	0.13	0.08	0.090	0.11	0.08
4	0.097	0.12	0.08	0.097	0.12	0.08	0.095	0.12	0.08
5	0.096	0.12	0.08	0.096	0.12	0.08	0.088	0.12	0.07
6	0.101	0.11	0.08	0.095	0.12	0.08	0.095	0.11	0.08

TABLE 15.—*Average Durations of Q R S Complex*

	Q R S_1			Q R S_2			Q R S_3		
Group	Average	High	Low	Average	High	Low	Average	High	Low
1	0.047	0.07	0.04	0.047	0.06	0.04	0.052	0.08	0.03
2	0.040	0.05	0.03	0.058	0.06	0.05	0.048	0.06	0.04
3	0.040	0.04	0.04	0.048	0.06	0.04	0.042	0.06	0.03
4	0.041	0.05	0.03	0.037	0.04	0.03	0.047	0.06	0.04
5	0.050	0.07	0.04	0.050	0.07	0.04	0.052	0.08	0.03
6	0.040	0.05	0.03	0.056	0.07	0.04	0.046	0.00	0.04

Seham's [17] average duration for the Q R S complex in full term infants, from 11 days to 1 year of age, is 0.036 second. Lincoln and Nicolson [22] found the Q R S complex to last 0.06 second in children from 3 to 12 years of age. In this series, no definite differences were found as regards age or lead. The shortest Q R S was 0.03 second, and the longest, 0.08 second. The general average was 0.04 second, this figure being 0.004 second higher than that given by Seham for full term infants (table 15).

22. Lincoln, E., and Nicolson, G. H. B.: The Hearts of Normal Children: III. Electrocardiographic Studies, Am. J. Dis. Child. **35**:1001 (June) 1928.

The characteristic short S-T or immediate take-off of the T wave in leads I and II seen in the premature infants in this study has been previously mentioned. The duration of the S-T interval was shortest in the second lead (table 16). This characteristic S-T interval seemed to persist in the older infants, although at times a definite S-T_1 or S-T_2 interval made its appearance (figs. 7 *B* and 9 *B*). The duration of S-T_1 and S-T_2 varied from 0 to 0.16 second, the general average being 0.056

TABLE 16.—*Average Durations of the S-T Interval*

	S-T_1			S-T_2			S-T_3		
Group	Average	High	Low	Average	High	Low	Average	High	Low
1	0.047	0.16	0	0.036	0.12	0	0.090	0.24	0
2	0.084	0.12	0.06	0.028	0.08	0	0.045	0.12	0
3	0.068	0.12	0	0.040	0.08	0	0.105	0.12	0.08
4	0.038	0.07	0	0.015	0.07	0	0.070	0.12	0
5	0.038	0.12	0	0.014	0.07	0	0.104	0.20	0.07
6	0.066	0.12	0	0.031	0.07	0	0.070	0.12	0

TABLE 17.—*Average Durations of T*

	T_1			T_2			T_3		
Group	Average	High	Low	Average	High	Low	Average	High	Low
1	0.163	0.24	0.08	0.174	0.24	0.08	0.101	0.18	0
2	0.114	0.16	0.05	0.168	0.20	0.12	0.140	0.24	0
3	0.130	0.20	0.09	0.160	0.20	0.12	0.074	0.12	0
4	0.147	0.20	0.09	0.181	0.24	0.13	0.091	0.18	0
5	0.148	0.20	0.07	0.150	0.22	0	0.052	0.12	0
6	0.146	0.20	0.10	0.156	0.20	0.10	0.080	0.16	0

TABLE 18.—*Average Durations in Lead II for Heart Cycle, Electrical Ventricular Systole, Electrical Ventricular Diastole and Heart Rate*

	P-P_2			Q R S T_2			Diastole			Lead 2		
Group	Average Heart Cycle	High	Low	Average	High	Low	Average Ventricular	High	Low	Average Rate	High Rate	Low Rate
1	0.475	0.540	0.420	0.267	0.28	0.22	0.202	0.245	0.160	159	178	147
2	0.457	0.485	0.410	0.246	0.27	0.20	0.211	0.240	0.180	169	196	150
3	0.405	0.450	0.360	0.252	0.28	0.24	0.152	0.210	0.120	183	200	158
4	0.383	0.420	0.345	0.247	0.28	0.22	0.137	0.160	0.105	198	230	176
5	0.412	0.460	0.360	0.241	0.28	0.20	0.171	0.210	0.135	182	214	158
6	0.417	0.520	0.305	0.245	0.32	0.20	0.169	0.220	0.105	186	250	143

second for S-T_1 and 0.027 second for S-T_2. This tendency for an immediate take-off of the T wave seems to persist in childhood as evidenced by the statement of Lincoln and Nicolson [22] that it was frequently impossible to measure the S-T interval in their series, consisting of children from 3 to 12 years of age. The S-T_3 interval, however, was frequently well developed wherever a T_3 was present (fig. 9 *A*), although at times in this lead also the interval was absent. The duration of S-T_3 fluctuated between 0 and 0.24 second, the general average being 0.153 second.

The duration of T in all three leads was longer in young than in older infants (table 17 and figs. 7, 8 and 9). The average durations were longest in the second lead, while T_3, which was frequently absent or of short duration, had an average duration about one-half that of T_2.

The duration of the complete heart cycle was longest during the first days of life (table 18). It diminished during the second week and continued to diminish as the infants grew older, and the pulse rate apparently increased. The average difference between pulse periods was 0.03 second (Seham [17] found a difference of 0.04 second in his cases). The duration of Q R S_2 varied between 0.241 and 0.252 second with

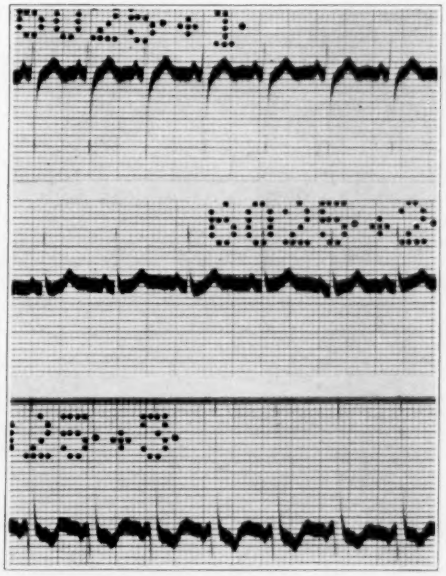

Fig. 10.—Electrocardiographic record taken at the age of 3 days.

the exception of the first days of life. During the first week Q R S T_2 averaged 0.256 second, and after this it averaged 0.246 second. Seham [17] found, in his series of full term infants, that the Q R S T phase measured 0.211 second in the new-born and 0.247 second in infants from 11 days to 1 year of age. The ventricular diastolic period, however, varied between 0.137 and 0.211 second, so that with the increase in pulse rate, the diastolic phase is shortened much more than is the systolic, as is well known.

Arrhythmias.—Krumbhaar and Jenks [21] found distinct sinus arrhythmias to occur for the first time at 6 weeks. Sinus arrhythmias were infrequent in the younger infants of Seham's [17] series. On using the same standard difference as these authors, i. e., a difference

between the longest and the shortest heart cycle of 0.1 second or more, we obtained 5 records (figs. 9 and 10) showing sinus arrhythmias. The ages of the infants showing these arrhythmias were 10, 12, 21, 90 and 101 days. The arrhythmias did not appear to be respiratory, the changes in rate taking place gradually. The follow-up records for two of the younger infants showing sinus arrhythmias showed a persistence of the arrhythmia in one and its disappearance in the other. (We do not have a follow-up record of the patient 10 days old.)

Extrasystoles in younger infants have been mentioned by Smith [20] and Burghard and Wunnerlich.[18] We observed two records showing auricular extrasystoles. One of them was of an infant 7 days old;

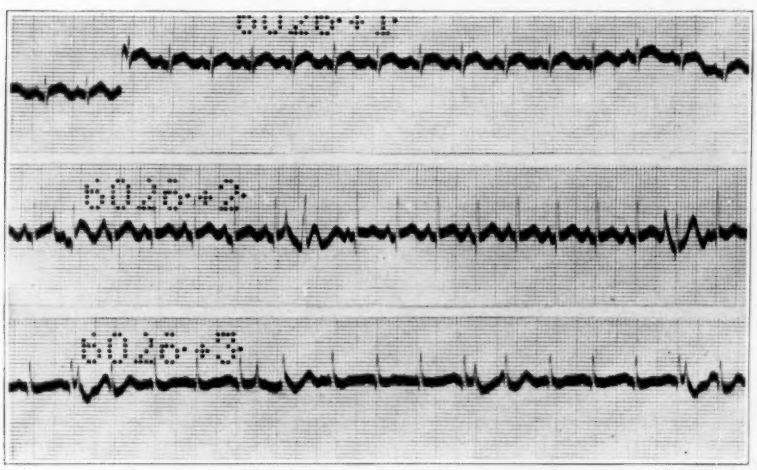

Fig. 11.—Electrocardiographic record taken at the age of 7 days.

a subsequent record, taken at 5½ months, did not show extrasystoles. The other was of an infant 5 months old; the early record in this case showed no extrasystoles.

Unusual Records.—The following description (fig. 11) of the record of the first case mentioned in the preceding paragraph was made by Doctor L. N. Katz:

The extrasystoles are characterized by spike-like deflections shorter and much taller than the usual P waves. They occur at varying phases in diastole; one in lead III starts before QRS is complete, indicating that the refractory period of the auricle is at the most 0.2 sec. Once, in lead 2, this is followed by a premature ventricular complex; the other auricular complexes are blocked. In several instances there is nodal escapement following the extrasystole. A most unusual circumstance, which we have never seen described in the literature, is the fact that these contractions are followed by undulations of the string at a frequency of about 200 cycles a minute. These undulations consist of from one to four waves. They

show a progressive decrease in amplitude, such as is seen in the decay curve of a freely swinging body. They may indicate that a transient flutter of the auricles has been set up.

Two records showed left axis deviation instead of the usual right; one is shown in figure 9. One of the records was from an infant 21 days old weighing 2,070 Gm., and the other from an infant 51 days old weighing 2,150 Gm. The follow-up record in the first case showed a shift to the usual appearance of the electrocardiogram. We obtained no later record on the second infant. There was nothing clinically to explain the unusual shift.

A rather interesting electrocardiogram (fig. 10) was obtained from the infant with persistent hypertension mentioned in the section on blood pressure. The electrocardiogram was taken when the infant was 3 days old and weighed 2,330 Gm. The usual right axis shift was present. The Q R S complex was spread, measuring Q R S_1, 0.108 second; Q R S_2, 0.06 second, and Q R S_3, 0.08 second, as compared with the averages for this infant's group: 0.047, 0.047 and 0.052 second, respectively (group 1). The S-T take-off was negative in leads I and III, contrary to the usual findings. The amplitudes were rather high in leads I and III, and there was slurring. Apparently we are dealing in this case with an intraventricular block.

Many of the records showed frequent fine waves due probably to muscle twitchings.

Pulse Rate.—As far as I know no statement concerning the heart rate in premature infants occurs in the literature. Lesne and Binet [3] found the pulse rate in full term infants at birth to be 150. This rate dropped to about 100 and then increased to 150 by the second day. Balard [23] obtained the same figures and stated that the pulse rate fell with the fall in body temperature. Smith,[20] obtaining his results from electrocardiographic studies on full term infants, found the following: the first hour the pulse rate was 122; from 10 days to 5 weeks it was 156; from the fifth week it was 135. Moving increased the rate to 160.

As a rule, we were able to count the pulse rate on the first day of life by means of cardiac auscultation. During the first day, on many occasions, the pulse rate was apparently not affected by crying or moving. No correlation between body weight and pulse rate could be made. The average pulse rate for the first day of life was 139 with rather wide fluctuations, although 75 per cent of the figures fell between 124 and 148. A high rate of 184 and a low rate of 106 were noted.

The rates on the electrocardiograms taken during the first two weeks of life averaged 163. This figure was obtained from records taken on infants resting quietly. The rate in the later groups averaged 182, and

23. Balard (footnotes 4 and 5).

wide fluctuations were noted. The highest rate was 261, and the lowest was 147. The value of the last average figure is questionable, since although the older infants were quiet when the records were taken, they had frequently been crying, moving or nursing just before the electrocardiograms were made.

III. ROENTGENOGRAMS OF THE HEART

No reference to the appearance or measurement of the heart of the premature infant as seen by the x-rays could be found in the literature. Walsh [24] measured the heart of the full term infant as seen on the roentgenogram; he also found that the heart and chest types do not change with age.

METHOD

The results reported in this section were obtained from a study of the roentgenograms of the chest of twenty-three premature infants; twelve were girls and eleven boys. Six of the infants were colored. The earliest plates were taken at 2 days of age, the latest at 5 months and 13 days. The weights varied from 1,815 to 2,445 Gm., when the first plates were taken, to 2,500 to 7,000 Gm., when the follow-up roentgenograms were made. The roentgenograms were taken at 30 inches (76.2 cm.), at the end of inspiration, with the infants lying prone. The distortion at this distance was not any greater than at 36 inches (91.4 cm.). Anteroposterior views were taken. Although we realize that this method was not the ideal one, it was the best one we had at hand.

TABLE 19.—*Heart Measurements*

No. of Cases	Weight, Gm.	Average Transverse Heart Diameter	Average Transverse Chest Diameter	Heart Diameter / Chest Diameter
7	1,800-2,100	4.1 cm. (3.5-4.4 cm.)	8.3 cm. (7.9- 8.8 cm.)	49.4% (44.2-52.4%)
19	2,100-2,500	4.6 cm. (4.2-5.0 cm.)	8.8 cm. (7.5- 9.8 cm.)	52.2% (49.3-58.3%)
4	2,500-3,500	5.2 cm. (5.2-5.5 cm.)	10.9 cm. (9.3-11.7 cm.)	47.7% (44.5-55.9%)
6	3,500-7,000	6.0 cm. (5.5-6.8 cm.)	12.0 cm. (10.3-13.5 cm.)	50.0% (45.8-58.2%)

RESULTS

The measurements were grouped according to weight and are shown in table 19.

Reference to table 19 reveals that the average transverse heart diameter increases with weight, the figures being 4.1 cm. in the lightest group of infants and 6 cm. in the heaviest. No correlation could be made with age. The relation of heart diameter to chest diameter varied from 47.7 to 52.2 per cent, the general average being 49.4 per cent. However, in twenty-seven (75 per cent) of the thirty-six plates this proportion was 50 per cent or more. The heart diameter to chest diameter ratio showed no tendency to stay the same in all cases, increas-

24. Walsh, J. F.: Chest of Newborn, Am. J. Roentgenol. **24**:140, 1930.

ing in some and decreasing in others. We did not have enough figures to compare the sexes.

The heart contour did not change with an increase in age in this series, the usual shape being pearlike. It might be mentioned that the infant with hypertension discussed in the previous two sections had a large heart roentgenologically, the heart-chest diameter ratio being 58.8 per cent.

SUMMARY

SECTION I

1. A study of the blood pressures of seventy-eight premature infants was made; a recording oscillometer with a small double cuff applied to the thigh and leg was used.

2. Weight is the most important factor influencing "basal" blood pressure. The systolic, diastolic and pulse pressures increase with a gain in weight. The diastolic pressure changes the least. This relationship exists up to a weight of 3,500 Gm. Beyond this weight no correlation can be made.

3. Regardless of weight, the systolic pressure was lowest, on the average, the first days of postnatal life.

4. Infants weighing less than 2,000 Gm. have lower systolic pressures than full term infants of the same postnatal age. Infants weighing over 2,000 Gm. have the same or higher systolic pressures than full term infants of the same postnatal age. The diastolic pressures were lower than those of full term infants.

5. No correlation could be made between the blood pressure level and the following factors: degree of prematurity, body length, race, circumference of thigh and leg, body temperature and time of day. Sleep caused a fall in systolic blood pressure in only 44 per cent of the cases observed. Feeding and crying each caused a rise in systolic blood pressure in only 40 per cent of the cases observed.

6. A case of hypertension in a premature infant was described. An increased systolic pressure was observed in four of the nine infants born of hypertensive mothers. Only one of the premature infants who died during the first four days of life had a systolic pressure lower than average.

7. Spinal puncture caused a drop in systolic pressure five of seven times.

8. Syphilitic premature infants, with one exception, did not show a persistent hypotension.

SECTION II

1. Electrocardiograms were analyzed in twenty-five premature infants.

2. The P waves in leads I and II tended to have a peaked form and to be relatively high throughout. P_3 was low, and at times was absent or inverted. In the older infants there was a tendency for the P waves in leads I and II to spread out, although the peaked form may persist.

3. A right axis deviation was found in this series with a few exceptions. The shift to an upright Q R S in lead I occurred at from 1 to 3 months of age in this group of infants, with two exceptions. Q R S was highest in lead III in the first two months of life. From the third month, Q R S was highest in lead II.

4. A high short S-T interval followed by a positive T was frequently present in leads I and II early in infancy. $S\text{-}T_3$ was frequently isoelectric and longer than in leads I and II.

5. The T wave in leads I and II tended to be broad in the early records, and later tended to abbreviate. T_3 was frequently absent or inverted, and when upright had a relatively low amplitude.

6. The amplitude of the deflections in general tended to be low in the early records and relatively higher in later records.

7. The durations of P_1 and P_2 were approximately equal, and both tended to increase with age. They varied from 0.039 to 0.058 second. The duration of P_3, which was the shortest, did not vary much with age, and ranged from 0.036 to 0.042 second.

8. $P\text{-}R_1$ and $P\text{-}R_2$ averaged from 0.095 to 0.106 second, while $P\text{-}R_3$ was shorter, averaging from 0.085 to 0.095 second.

9. The average duration of the Q R S phase was about the same in all the groups and all the leads, and measured 0.04 second.

10. $S\text{-}T_1$ and $S\text{-}T_2$ were rather short. The former averaged 0.056 second in duration, and the latter averaged 0.027 second throughout. $S\text{-}T_3$ averaged 0.153 second.

11. The duration of the T wave in all three leads tended to be longer in the early weeks of infancy.

12. Both the complete heart cycle and the Q R S T were longer in the early records of infancy than they were in the later ones, which were taken when the pulse rate was much more rapid. With an increase in pulse rate, the electrical ventricular diastole was decreased much more than the electrical ventricular systole, as is well known to be the fact in adults.

13. Five cases of sinus arrhythmia occurring in infants from the ages of 10 days to 101 days were observed. The change in rate was gradual and unrelated to respiration.

14. Two cases of auricular extrasystole were observed, one with a peculiar appearance. Two records showed left axis deviation early; one infant had a record resembling that seen in intraventricular block.

15. There was no correlation between body weight and pulse rate. The average pulse rate the first day of life was 139. During the first two weeks it was 163. The later figure of 184 is probably not a good one because the infants had frequently been crying or feeding before the records were made.

SECTION III

1. The roentgenologic measurements and appearances of the hearts of twenty-three premature infants were analyzed.

2. The average transverse heart diameter increased from 4.1 cm. in the lightest group of infants to 6 cm. in the heaviest.

3. The relation of the heart diameter to the chest diameter averaged 49.4 per cent. However, in three fourths of the plates this ratio was 50 per cent or more.

4. The heart contour showed no changes with an increase of age and weight, but was pear-shaped throughout.

The analyses of the electrocardiograms were checked by Dr. L. N. Katz, whose advice and guidance in carrying out the whole problem were extremely valuable.

Miss Evelyn Lundeen, R. N., cooperated in the premature station and the follow-up clinic, and Miss Bessie Phillips aided in making the electrocardiographic records.

A RESTRAINING GARMENT TO BE USED IN THE TREATMENT OF CHILDREN

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SANTA BARBARA, CALIF.

All doctors and nurses working with children appreciate the fact that when it is necessary to carry out certain measures, such as diagnostic procedures and treatments, it is absolutely essential to have the patient restrained in such a manner that the attention of those in attendance may be directed to the work at hand rather than to holding the child. At times I have seen a comparatively small child resist a minor procedure sufficiently to require the assistance of four or five nurses in order that the doctor might work, and even then it was difficult to do good work. Such cases are very trying to both the patient and the attendants. When necessary for some procedure to be done, it is much more humane and much more simple if the patient is restrained beyond all question of doubt.

My observations have been that in most institutions a child to be restrained is rolled securely in a blanket or a sheet, and that safety pins are used to keep him confined. It was after several such cases, during which procedure I pricked my finger with a safety pin—once after taking blood in a suspected case of syphilis—that I decided to do away with pins in the future, and had a garment made that was easy to operate.

The drawings and photographs are nearly self-explanatory. The garment [1] is made of heavy canvas and is sufficiently large to take care of an older child. Because it is freely flexible, a child of any age may be confined by merely drawing the straps tightly and allowing the canvas to fold. The garment is placed on a table, and the child, not knowing what is to happen, is placed in it. The zipper is then closed quickly, and the battle is over. The straps are placed in such a way that one binds the arms just below the shoulders, one the wrists, one the knees and one the ankles. When securely strapped, the child can move only the head, and, to prevent possible doubling up, steel bars are enclosed down the back on each side. These may be removed if the garment becomes contaminated and is to be put in the autoclave. The drawing gives the various dimensions.

1. This garment was made by Mrs. Flo Cox, 1333 Bath St., Santa Barbara, Calif.

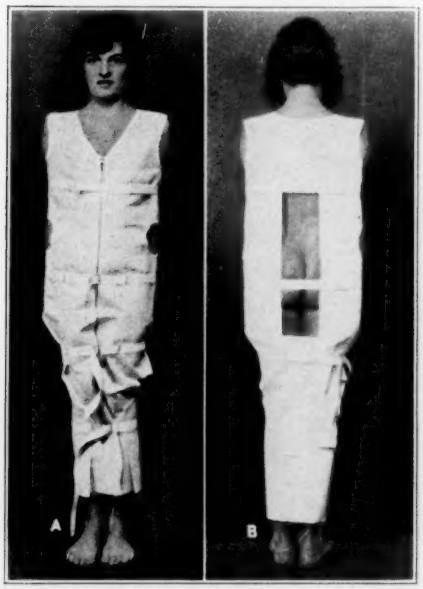

Fig. 1.—*A*, front view, with all extremities confined. *B*, rear view, showing a window in the lumbar region.

Fig. 2.—*A*, patient restrained except for right arm. *B*, patient restrained except for right leg.

Figure 1 *A* gives a front view, with all extremities confined, the position necessary when work is to be done on the patient's head. The head is easily held in position by one assistant. This method has been used to examine the ears and throat, to remove foreign bodies from the ears and nose, for gastric lavage in cases of poisoning and for opening an acute cervical abscess.

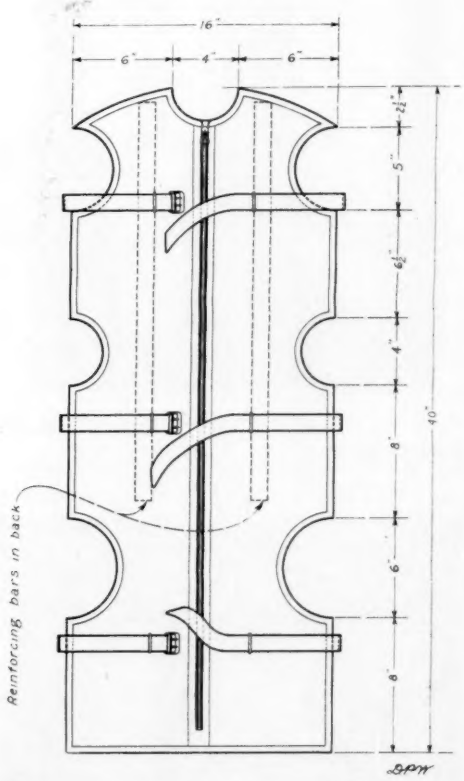

Fig. 3.—Diagrammatic sketch of garment, giving measurements.

Figure 1 *B* gives the back view, showing a window in the lumbar region. A spinal puncture is easily done while the patient is held on the edge of the bed by one assistant.

Figure 2 *A* shows the patient restrained except for the right arm. This position is used for giving transfusions, for venal puncture, for giving intravenous serums, for opening abscesses and for other necessary treatment for conditions of the upper extremities.

Figure 2 *B* shows the patient restrained, except for the right leg. This is of value in any treatment such as opening an abscess of a lower extremity. The openings in the middle of the garment are for the lower extremities of small children.

A frame to be used in the treatment of infants was described by Laird.[2] Undoubtedly, other physicians may have used and described such a garment as this one, but if so I have never seen the descriptions, and I feel that others would welcome a simple device to help them in the treatment of their patients.

Santa Barbara Clinic

2. Laird, Archibald: A Frame to be Used in the Treatment of Infants, Am. J. Dis. Child. **41**:1307 (June) 1931.

Case Reports

ALEUKEMIC, MYELOGENOUS CHLOROMA

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HASTINGS, NEB.

Since Burn's original description in 1823, chloroma has been the subject of periodic reviews, the more important of which include those of Dock and Warthin,[1] Lehndorff,[2] Burgess,[3] Brannan [4] and Washburn.[5] Washburn collected 162 cases of chloroma between 1823 and 1929. The earlier observers considered the disease to be lymphogenous, but since the advent of the oxydase reaction most investigators have come to regard it as being myelogenous. Washburn did not feel that it was possible to deny the existence of a lymphoid type. Brannan, however, classed chloroma as "some variety or form of myelogenous leukemia," and discounted entirely the probability of the occurrence of the lymphatic type of the disease. Moreover, Brannan concluded that the aleukemic form of chloroma was exceedingly rare.

The following case of aleukemic chloroma was considered sufficiently unusual to warrant its publication.

CASE REPORT

History.—A white girl, aged 2 years, was first seen on June 5, 1931, because of bilateral exophthalmos. On May 12, 1931, the mother had noted that the child's upper lids were ecchymotic. For two weeks the hemorrhagic discoloration of the lids increased, and in the third week both eyes were surrounded by ecchymoses, the lids were edematous, and there was bilateral exophthalmos. There had been no subjective signs of illness and no interference with appetite or sleeping. Both the familial and past histories were unimportant.

Physical Examination.—The child was well nourished and alert and felt well. The exophthalmos was equally well developed in both eyes, and there was evidence

1. Dock, G., and Warthin, A. S.: A New Case of Chloroma with Leukemia, with a Study of Cases Reported Since 1893, M. News **85**:971, 1904.

2. Lehndorff, H.: Chlorom, Ergebn. d. inn. Med. u. Kinderh. **6**:221, 1910.

3. Burgess, A. M.: Chloroma, J. M. Research **22**:153, 1912-1913.

4. Brannan, D.: Chloroma; The Recent Literature and a Case Report, Bull. Johns Hopkins Hosp. **38**:189, 1926.

5. Washburn, A. H.: Chloroma, Report of a Case with Recovery Following Roentgenotherapy, with a Review of the Literature, Am. J. Dis. Child. **39**:330 (Feb.) 1930.

of both old and recent subcutaneous hemorrhage into the lids. The upper lids were more edematous than the lower, and there was a soft swelling of the subcutaneous tissue above and lateral to the orbits. There was a small, rounded, indefinitely outlined elevation of the skin in the left temporal region which was soft and not fixed to the skin.

There was no impairment of hearing or vision. The ocular movements were unimpaired and the pupillary reflexes normal. There was no paralysis or weakness of the facial muscles. Examination of the nose, throat and ears gave negative results.

There was no palpable lymphadenopathy.

The chest was well developed and symmetrical, and the costochondral junctions were normal. The lungs were normal; the heart was not enlarged or displaced, and the pulse was regular and of good volume. The abdomen was rounded and there were no palpable abnormalities. The genitalia and extremities were normal.

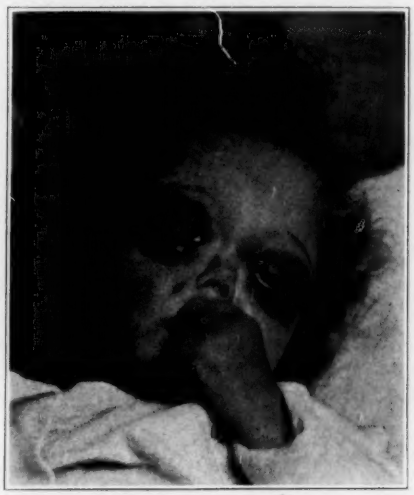

Fig. 1.—Appearance of patient three weeks before death.

Although no abnormal reflexes were elicited, the child suffered from what seemed to be periodic attacks of vertigo, at which times she would fall. These lasted only a few minutes and presented no objective symptoms, other than the falling.

The temperature was normal.

Course.—On June 6, there was a small submucosal hemorrhage and swelling of the left side of the hard palate, and on June 8 a similar finding on the right side.

Mucosal hemorrhage in the hard palate became more pronounced with progressive obliteration of the arch of the palate by soft, submucosal tumor masses. The tumor in the left temporal region became larger, and the exophthalmos became progressively more marked.

On June 15, eleven days after admission, there was slight bleeding from the nose, which continued intermittently throughout the course of the disease. The nose became completely obstructed and the soft palate depressed. There was palpable cervical lymphadenopathy and a palpable tumor to the left of the midline in the upper part of the abdomen.

The child died on July 19, sixty-eight days after the onset of symptoms. Although there had been some continuous bleeding from the nose, the amount of blood lost was not considered significant. The day before death there was a rather severe hemorrhage from the mouth of about one hour's duration. For several weeks prior to death there had been increasing respiratory difficulty. The nose was completely obstructed, the arch of the palate was obliterated, the tongue was pushed forward, the mandible was fixed, and there was massive cervical lymphadenopathy.

Laboratory Examination.—Urinalysis was repeatedly negative. The results of examination of the blood are recorded in the accompanying table. Blood smears were stained on three occasions by the oxydase method, and the majority of the cells were oxydase-negative. Anisocytosis and poikilocytosis were consistently seen in the red blood cells. A few normoblasts were seen on two occasions.

Treatment.—Roentgen therapy was instituted on June 12, at which time one half of an erythema dose was given to the left temporal region. This was repeated on June 14 to the right temporal region and on June 30 to the upper part of the abdomen. Following the first treatment there was a slight transient diminution in the exophthalmos and in the palpebral edema.

The Results of Examinations of the Blood

	Red Blood Cells	Hemoglobin	White Blood Cells	Polymorphonuclears, per Cent	Myelocytes, per Cent	Lymphocytes, per Cent	Monocytes, per Cent
June 5	2,680,000	45	10,160	25	0	60	15
June 13	.....	40	7,600				
June 17	.....	..	.....	30	0	62	8
June 22	.....	..	.....	21½	½	70	8
June 25	2,000,000	30	7,500				

On June 15, 5 cc. of the mother's blood was injected intramuscularly. On June 17, 7 cc. was injected, and on June 19, 22, 24, 27 and on July 1, 8 cc. was injected. No beneficial effects were noted.

Autopsy.—I performed the autopsy six hours after death. The body was that of a pale white female infant. The circumference of the head was increased asymmetrically. The lids could not be closed. The skin of the face and neck was blue, and there was extensive old and recent hemorrhage into the lids and skin around the eyes. The inferior border and rami of the mandible were obscured by the cervical tumor masses which were soft and indefinitely outlined. There was bloody discharge from the nose and mouth. The superficial cervical veins were distended.

The skin and subcutaneous tissue were edematous and elevated over nodular, hemorrhagic tumor masses which were attached to the bone. Almost the entire skull was covered in this manner. The outer table to which the tumor masses were attached was partially destroyed, had a honeycombed appearance and was friable. The tumor tissue cut with ease, did not collapse and had the appearance of a partially organized hematoma. The tumor masses were most luxuriant along the suture lines where they were continuous with subdural tumor masses of similar character. The subdural tumors were most prominent at the base, where they continued through the orbital fissures into the retrobulbar spaces, with extensive destruction of the left orbital plate The zygomatic, temporal and maxillary bones were similarly involved.

Other than the large masses of tumor apparently occupying the site of the cervical lymph nodes, there was no abnormality in the neck.

The normal relation of viscera obtained throughout the chest, and there was no abnormal collection of free fluid in the serous cavities.

The lungs were voluminous, crepitant throughout and free from pathologic change. The trachea, bronchi and pulmonary vessels showed no abnormality.

The thymus showed no gross abnormality.

The abdominal cavity was almost completely filled by an irregularly nodular, confluent, soft tumor mass which extended from the diaphragm to the bifurcation of the aorta in the midline. This mass had displaced the abdominal viscera to each side and resulted in a tilting forward of the liver. On section, it was found that this mass occupied the site of periaortic and retroperitoneal lymph nodes which were

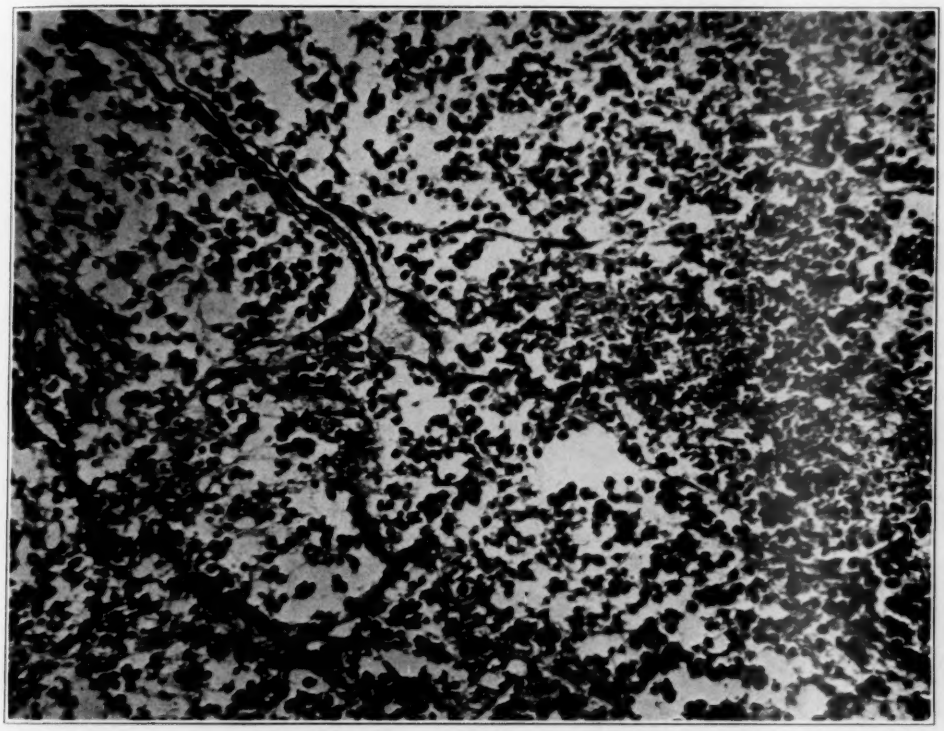

Fig. 2.—Photomicrograph of the tumor of the skull showing arrangement of the cells. The cells have relatively large nuclei, are indefinitely outlined and are supported on a scanty fibrous stroma. Hematoxylin-eosin; × 120.

coalescent and which encased the aorta and the inferior vena cava in a solid mass of tumor. This tumor was less hemorrhagic than the tumor masses on the skull and had a translucent, gray-green appearance.

The liver and spleen showed no evidence of pathologic change.

There were no gross abnormalities in the suprarenals, pancreas, kidneys, bladder or uterus. Both ovaries were enlarged, each measuring about 6 cm. in the long axis by 4 cm. in diameter. The surface of the ovaries was smooth, and on section both were entirely occupied by a tumor mass which in places was hemorragic and in others green and translucent. This tissue was friable, but not necrotic.

The gastro-intestinal tract did not show evidence of pathologic change.

Histologic Examination.—The tumor was composed of masses of apparently unattached cells which were supported on a delicate fibrous stroma. The cells varied in size, shape, distinctness of outline and staining characteristics. The predominant cell type was about 12 microns in diameter, round, and had a relatively large, dense chromatic nucleus. Chromatin was distributed unequally and tended to be concentrated in clumps. The cytoplasm was in some instances homogeneous and in some instances finely granular, but only rarely approached the degree of granularity seen in mature polymorphonuclear leukocytes. The cytoplasmic granules did not stain specifically with the Giemsa method, but by the oxydase method almost all of these cells showed the specific green reaction. There was considerable variation in the size of the nuclei, and mitoses were frequent. Occasional mature and immature leukocytes could be identified. Small giant cells with faintly staining cytoplasm and four or five deeply staining round nuclei were encountered. Occasional nucleated red cells were present. In the sections taken from the tumors of the skull there was extensive hemorrhage, and many vascular spaces were partially obliterated by tumor. The distribution of stroma varied. In places the tumor cells appeared to be unattached, while in other places they were supported by a fine, intercellular, acidophilic, fibrillar substance which was continuous with the definitely fibrous trabeculae that supported and separated the islands of cells. There were large areas of hemorrhagic necrosis.

Sections of the tumors of the skull, including the bone, showed the marrow spaces to be filled with tumor similar to that described. The cortex and periosteum had been invaded and destroyed. Fine radially disposed trabeculae of bone projected into the tumor and marked the site of the outer table of the skull.

Sections of retroperitoneal lymph nodes, of cervical lymph nodes and of ovaries and suprarenals showed the presence of tumor similar to that described in the skull. The tumor in the ovaries showed less vascularization, less hemorrhage and less necrosis, but its cellular components and structure were similar to those already described. The metastases in the suprarenals were found in the medulla. Tumor tissue had completely supplanted the normal architecture in the lymph nodes.

Routine examination of other viscera showed: The liver and kidneys were the seat of a moderate degree of parenchymatous degeneration with fatty degeneration of the former. There was no evidence of pathologic change in the lungs, heart, spleen or gastro-intestinal tract.

The oxydase reaction was positive on sections of tumor tissue from skull and ovaries. Almost all of the cells constituting the tumor took the specific stain for granulocytes. No additional information was gained from sections stained by the Giemsa method.

SUMMARY

A case of chloroma occurring in a girl 2 years of age and terminating in death within sixty-eight days after the onset of symptoms has been described. Profound anemia was present when the patient was first examined, twenty-three days after the onset of symptoms, and progressed in severity to the time of death. Roentgenograms of the long bones taken one month after the onset of the disease did not indicate a generalized involvement of bone marrow. Repeated examination of the blood failed to disclose any leukemic changes. The tumor was primary in the bones of the skull, with early production of exophthalmos, and metas-

tases were present in the lymph nodes, ovaries and suprarenals. Both the primary and the secondary tumors gave a strongly positive oxydase reaction. The characteristic green color was obscured in the primary tumors by necrosis and hemorrhage, but was typical in the metastases.

Roentgen therapy was instituted within a month after the onset of symptoms, with no beneficial effects.

MASSIVE INTRA-ABDOMINAL HEMORRHAGE IN THE NEW-BORN

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BROOKLYN

With the increasing acceptance of the care of the new-born by the pediatrician, problems that receive casual mention in the larger textbooks deserve emphasis in pediatric periodicals. This is true of the subject under consideration in this paper. Two cases of massive intra-abdominal hemorrhage were observed in autopsies that I performed within a period of ten months, in a service in which the average rate per month of admissions to the nursery is ninety. This experience stresses the importance of watchfulness for this condition.

REPORT OF CASES

CASE 1.—Infant B., a girl, was admitted to the Coney Island Hospital on Sept. 17, 1930, with a history of normal delivery by a midwife. Respiration had not commenced immediately, and the manual method of resuscitation was utilized by the midwife, who placed both thumbs under the ribs and pushed upward toward the chest. The exact position of her thumbs is indicated in figure 1 *A* and *B*, where subcapsular hemorrhages of the liver took place.

Examination on admission, which was three hours after delivery, revealed a large, well nourished, white, new-born girl. Her cry was vigorous. There was moderate cyanosis of the lips. The lungs were well aerated. The heart was normal. Physical examination gave essentially negative results. During the following three days, she nursed well, and no unusual conditions were noted. At 10 a. m. on September 21 she suddenly became pale and cyanosed. A cold clammy sweat appeared. The pulse was thready and rapid, and the respirations were shallow, rapid and noisy. Pulmonary edema followed, and within four hours she died.

Postmortem examination, which was performed three hours after death, revealed the following positive observations: marked pallor of the skin, mucous membranes and all visceral organs. On opening the peritoneal cavity about 350 cc. of clotted and unclotted blood was found. The liver (fig. 1) had the usual rhomboid form and light brown color. On the inferior anterior portion of the right lobe, there was a purplish discoloration extending over an area 4 by 7 cm. On the lower anterior border of this area, there was a rough stellate rupture through which fluid blood could be expressed. On incision, a cavity was revealed containing clotted and unclotted blood and measuring 3 by 5 cm. On the anterior border of the left lobe, a similar discoloration was noted, measuring 1.5 cm. in diameter. Incision through this area revealed a small cavity containing clotted blood and measuring 1 cm. in diameter.

CASE 2.—L, a boy, was delivered at the Coney Island Hospital on July 1, 1931, after a normal labor. He cried immediately and showed no abnormalities on physical examination. On the second and third days, no unusual features were observed. He nursed well, and his cry was vigorous. On the morning of the fourth day, he became extremely weak and refused to nurse. His breathing was rapid and shallow. On examination, a marked pallor of the skin and mucous membrane, and rapid, thready pulse were noted. Within a few hours, the patient died.

Postmortem examination was made on the following day. The important relevant observations were: There was marked pallor of the skin, mucous membranes and all visceral organs. The peritoneal cavity was distended with a large amount of clotted and unclotted blood. In the area of the right kidney there was a large

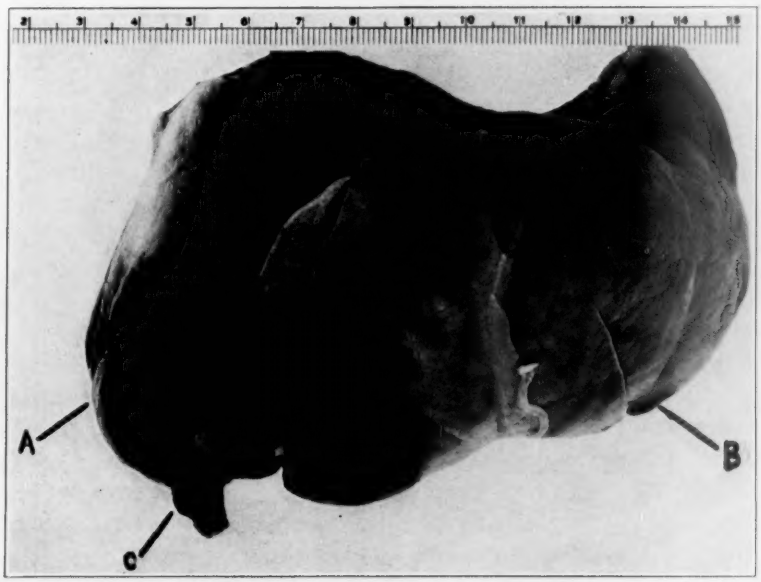

Fig. 1 (case 1).—The liver, showing: *A*, extensive intrahepatic hemorrhage in the right lobe, with formation of a large cavity and stellate rupture at *C* through which blood escaped into the abdominal cavity, and *B*, small intrahepatic hemorrhage in the left lobe, with formation of a small cavity containing blood.

elliptical purple mass which extended up behind the right lobe of the liver and downward into the right iliac fossa. On the anterior exposed surface of this mass, a stellate rupture about 1 cm. in diameter was present, through which the blood escaped into the peritoneal cavity. The entire mass, the right ureter, the bladder, the left kidney and ureters were dissected out. Cutting through this right-sided mass (fig. 2) revealed that the original hemorrhage occurred in the right suprarenal gland, distending and stretching the cortex into a thin layer surrounding a large clot of blood with a diameter of 3 cm, which replaced the medulla. Immediately beneath the suprarenal gland and enclosed in the same mass was the right kidney, the upper pole of which was flattened by the enlarged right suprarenal. Cut section of the kidney showed the usual structure and normal proportion between the cortex and the medulla. The perisuprarenal and perirenal tissues were infil-

trated with clotted blood. The left kidney, ureter and bladder showed the normal configuration. The left suprarenal was slightly thickened, and on section a small amount of blood was released. The medullary portion was partially replaced by a cavity which contained unclotted blood.

COMMENT

Exsanguination, due to massive intra-abdominal hemorrhage, was the direct cause of death in both cases. This was secondary to spontaneous

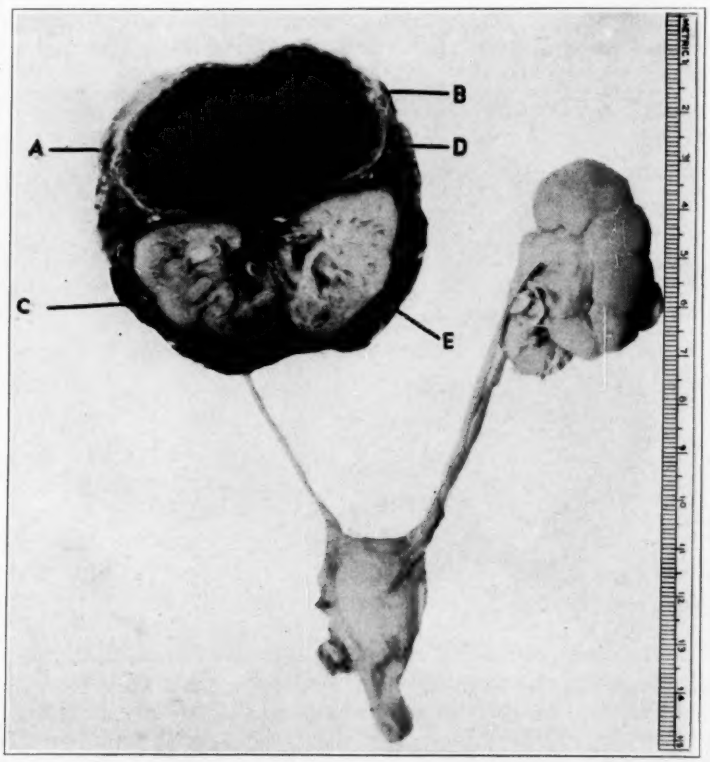

Fig. 2 (case 2).—Urinary system and right suprarenal gland. The mass is split in the middle and the two halves are spread, demonstrating, *A*, blood clot filling and replacing the medulla of the right suprarenal; *B*, thinned out cortex of the right suprarenal; *C*, right kidney (split); *D*, perirenal tissue infiltrated with blood, and *E*, perisuprarenal tissue infiltrated with blood.

rupture of a previously formed hemorrhagic cavity in an abdominal viscus. In the first case, the latter was the result of violent methods of resuscitation. The exact position of the midwife's thumbs pressing upward under the ribs is indicated by the intrahepatic hemorrhages. The patient showed no effects from this condition for three days. On the fourth day, when hemorrhagic tendencies in the new-born are greatest,

and possibly in addition because of ordinary handling of the infant during nursing or change of clothes, the hemorrhagic cavity in the right lobe of the liver became freshly distended and ruptured into the peritoneal cavity. The rapid succession of events leading to a fatal issue gave no opportunity for laboratory investigations, such as determinations of the bleeding time, coagulation time, platelet count or calcium content of the serum. Recent investigations have demonstrated that in hemorrhagic disease of the new-born, these laboratory tests are frequently negative, and that the main causative factor in this condition is the lack of, or poor quality of, the prothrombin enzymes, with resultant defective clot formation. Examination of the abdomen for fluid wave and shifting flat percussion note in the flanks, with rapid decrease of hemoglobin percentage determined by repeated tests, would have established the diagnosis of intra-abdominal hemorrhage. The best recommendation to prevent a recurrence of this situation, taught by this case, is to eliminate all forceful methods of resuscitation and the generalization of the use of the catheter cleansing of the throat, stimulation of the skin by cold and warm baths and occasional use of alpha lobeline. The time will come when every delivery room will be equipped with a small Drinker respirator, and many lives will be saved, and forceful methods of resuscitation will be a thing of the past.

The rapid respirations, dilating alae nasae and expiratory grunt influenced the intern on the service, in spite of the absence of pulmonary signs, to diagnose the second case as bronchopneumonia. Errors in the diagnosis of conditions in the new-born are pardonable, considering that the syndromes of most of these conditions include dyspnea, cyanosis, marked pallor, marked changes in the pulse and anorexia. These are possibly due to the instability of the nervous system in the new-born, with resulting marked reactions in both mild and severe conditions. Recent publications contain descriptions of characteristic syndromes in suprarenal hemorrhage. These include the foregoing signs (rapid respirations of the shallow type), also lowering of the blood pressure and occasionally the palpation of a mass in the region of the affected suprarenal gland. In my opinion, forceful palpation for a mass of this type is not without danger. With little pressure, the friable, distended and blood-soaked suprarenal gland will tear, and more bleeding will occur. The great variations in the experience of many observers indicate that a definite syndrome cannot be adopted as yet for suprarenal hemorrhage in the new-born. Diagnosis will be possible when quantitative tests for suprarenal internal secretions have been perfected. The vascularity of the suprarenal gland accounts for the frequency of involvement of this structure, owing to the increased hemorrhagic tendencies during the new-born period. Both cases occurred on the fourth day of life, and were

very likely associated with this hemorrhagic tendency. Other possible factors, such as asphyxia neonatorum, trauma from prolonged labor and resuscitation methods were not present in case 2. With such extensive involvement of both suprarenals (destruction of the entire right suprarenal and half of the left suprarenal), a fatal issue would very likely have occurred. Death was hastened by exsanguination when rupture of the gland took place and the blood filled and distended the peritoneal cavity. Rare instances of rupture of the suprarenals in the new-born have been observed and recorded in the literature. Diagnosis of hemorrhage into the peritoneal cavity could be made when signs of abdominal fluid are elicited in combination with decreasing percentages observed in repeated determinations of the hemoglobin.

SUMMARY AND CONCLUSION

Two cases of massive intra-abdominal hemorrhage in the new-born are described. In one case, the hemorrhage originated in the liver, where trauma due to forceful methods of resuscitation produced two subcapsular hemorrhages into the liver tissue. In the other case, the hemorrhage came from the right suprarenal gland, where a large intrasuprarenal hemorrhage preceded the abdominal hemorrhage. Both patients died on the fourth day of life, when the greatest incidence of hemorrhagic disease of the new-born occurs. This was considered an important factor.

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SPONTANEOUS GANGRENE OF THE EXTREMITIES

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The distressing uncertainty in regard to the etiologic factors leading to spontaneous gangrene [1] appears to be exemplified in the following case.

REPORT OF A CASE

History.—The patient, a girl, was born in Milwaukee, on Dec. 8, 1922, of Italian parents, at full term, following a difficult labor assisted by a midwife. The weight at birth was 3 pounds (1,360 Gm.). There was paralysis of the upper part of the left arm, which gradually disappeared. The head was not deformed. The father and mother were living and well. There were no other children. Two miscarriages preceded the birth of this child, and no pregnancies occurred later. There was no history of epilepsy, insanity or feeblemindedness in the family. The child talked when she was 1 year of age and walked when she was 16 months old. She had scarlet fever and measles. Otherwise development was uneventful and normal until December, 1926, when at the age of 4 years, she fell down a flight of stairs. This event marked the onset of periods of unconsciousness during which she would roll her eyes, shake all over and fall to the floor. In one of these falls she broke her nose. She did not bite her tongue or froth at the mouth. The attacks lasted for less than one minute. At first they occurred at intervals of from five to six hours, but they increased in frequency to several attacks in one hour.

The patient was admitted to the Children's Hospital, on May 13, 1927, for observation. The parents removed her, against advice, the following day. No diagnosis was made. On Jan. 22, 1929, she was again admitted to the Children's Hospital for study of the convulsive state.

Examination.—The cervical glands were palpable. The thyroid gland, the heart, the skin and the extremities were normal. There was definite mental retardation. There were crackling râles in the bases of both lungs. Urinalysis gave negative results. Examination of the blood showed: red blood cells, 4,620,000, and white blood cells, 12,000; hemoglobin, 83 per cent; polymorphonuclears, 60 per cent; small lymphocytes, 31 per cent; large lymphocytes, 4 per cent, and eosinophils, 4 per cent. The blood calcium was 12.03 mg., and the phosphorus, 4.9 mg., per hundred cubic centimeters. The Wassermann reaction was negative. The temperature ranged from 102 to 103.2 F. The pulse rate was from 100 to 120; the respiratory rate was 25.

A very definite respiratory infection was present. A roentgenogram showed a brachycephalic skull with a shallow anterior fossa and a deep middle posterior fossa. The outline of the sella, the sutures and the thickness of the skull were normal. The shadows of the blood vessels were very inconspicuous. All of the findings were normal.

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1. Lewis, Dean: Spontaneous Gangrene of the Extremities, Arch. Surg. **15:** 613 (Oct.) 1927.

Course.—The patient was again removed from the hospital, against advice; she had an active respiratory infection and a temperature of 103.2 F. She walked downstairs to the front door of the hospital and was taken across the city to her home in a taxicab, in her bed-clothes, with a blanket thrown over her, at 5 p. m., January 31, seven days after admission. The official atmospheric temperature at the time was 3 degrees above zero.

The same evening, shortly after her arrival home, pain developed in the legs and feet, which gradually became excruciating, and the child screamed in paroxysms of pain. From the knees down the legs were hot, red and somewhat swollen. (I am quoting the parents.) The child repeatedly begged them to put the legs in cold water.

The family physician was called three days later, and found blotches, confluent purpuric areas in both legs extending over the feet; the hair follicles were prominent, and the epidermis resembled pig skin. It became gradually transparent and parchment-like. At the end of a week there was no line of demarcation, and the

Photograph of patient with spontaneous gangrene of the legs.

muscles of the feet still functioned. The tissues were dry at all times. Other physicians saw the patient during this period. One tentative diagnosis of acute Raynaud's disease was made. I first saw the child on March 11; both legs were dead below the knees, with a slough at the line of demarcation extending to the bones, with a fetid local infection. My first impression was that the limbs had been frozen. The legs were amputated three days later, the right one was disarticulated at the knee and the left amputated at the junction of the middle and upper third of the tibia. Both popliteal arteries were pulsating. Skin traction was applied and closure effected some days later. Healing and convalescence were uneventful. The arteries and veins were dissected from the amputated extremities with difficulty. They were adherent to the adjacent tissues and to each other. Microscopic examination showed thrombosis of both arteries and veins, with beginning organization of the thrombus. The tissue around the vessels showed inflammatory infiltration. Dr. Grill gave his assistance in securing and preparing the tissue.

Postoperative Course.—On July 2, 1931, the patient weighed 150 pounds (68 Kg.) and had loss of consciousness of a few seconds' duration several times an hour. There were a slight change of the facial expression and widening of palpebral clefts. There were no real convulsions.

Buerger [2] described thrombo-angiitis obliterans as an acute inflammatory lesion with occlusive thrombosis. The earliest changes are evidences of acute inflammation, involving all the coats of the vessel. The media, adventitia and perivascular tissues are infiltrated with polymorphonuclear leukocytes, and the lumen is filled with a red clot. Then occur the formation of miliary giant cell foci, the organization and canalization of the clot, the disappearance of the inflammatory products and the development of fibrotic tissue in the adventitia that binds together the artery, vein and nerves. He stated that the early lesions are rarely seen in the deep vessels, because the patients do not allow amputation until the disease has lasted for several months or years. The process affects the veins to the same extent as the arteries. An interesting change is the fibrotic thickening of tissues immediately about the vessels, an agglutinative process that binds together the artery and its collateral veins.

In his series of 1,000 cases, Buerger found the condition widespread among many nationalities. He reported only three cases occurring in females; the youngest patient was 17 and the oldest 56 years. He expressed the belief that though the disease is of inflammatory origin, no causal agency has been discovered as yet, and that when acute infections are mentioned, it is more likely that the condition is a complicating thrombo-arteritis and not a true thrombo-angiitis, and that when symptoms comparable to those of thrombo-angiitis develop after exposure to thermal influences, thrombotic processes the pathologic nature of which is quite different from thrombo-angiitis are likely to occur.

Allen and Brown [3] in February, 1928, in an extensive series of cases, made observations similar to those of Buerger, except that they found that evidence of acute inflammation was extremely rare, and that proliferation of the intima seemed out of proportion to the age of the patient. They found that only three of two hundred patients were free from a demonstrable focus of infection. The youngest patient was 17 and the oldest, 64.

Cahill [4] reported a case in a Jewish boy, aged 2 years, in which occlusive thrombi developed in the vessels of both feet following the development of a furuncle on the neck. He believed it to be a case of bilateral thrombo-angiitis obliterans with an acute onset.

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2. Buerger, Leo: Thrombo-Angiitis Obliterans, in Nelson: Loose-Leaf Living Surgery, New York, T. Nelson & Sons, 1927, vol. 3, p. 755.

3. Allen, E. V., and Brown, G. E.: Thrombo-Angiitis Obliterans: Clinical Study of 200 Cases; Etiology, Pathology, Symptoms, Diagnosis, Ann. Int. Med. **1**:535 (Feb.) 1928.

4. Cahill, J. A., Jr.: Thrombo-Angiitis-Obliterans; Report of Acute Case in Child of 2 Years; South. M. J. **21**:105 (Feb.) 1928.

Dean Lewis [5] said that spontaneous gangrene occurs in the relatively young and in the old, justifying the clinical classification of senile and presenile gangrene, one dependent on degeneration and the other on inflammation superimposed on arteritis or, because of the almost constantly associated involvement of veins, thrombo-angiitis. Extending the degenerative or senile type to cases involving thickening of the intima and sclerosis and calcification, there appears to be a definite group of changes associated with a presenile type.

In 1878, von Winuvarter [6] published pathologic observations in cases in which practically all the arteries of the leg were obliterated by a proliferative process apparently originating in the intima. He called the condition endarteritis obliterans, an inflammation of the walls of the vessels with thrombus formation followed by organization and canalization. In this type (I am quoting Lewis), arteritis, periarteritis, phlebitis and periphlebitis, because of the frequent concomitant association of veins and arteries in the process, are the initial lesions, and the name thrombo-angiitis is probably a more appropriate term. It would seem that a thrombo-angiitis may have various early manifestations, such as dysbasia and symptoms suggestive of deep vessel involvement, or the first indication may be the appearance of trophic changes. Lewis stated that one of the most striking changes in thrombo-angiitis is the extensive collateral circulation that may develop, and quoted Meleney and Miller [7] as stating that if the disease continues instead of subsiding, a contest develops between the two forces. Lewis described at length a case in which the general arterial tree was extensively involved without marked functional disturbance because of the compensatory development of the collateral circulation.

Austrian,[8] in discussing pneumonia, mentioned venous thrombosis occurring in 5 per cent of a large series of cases of acute lobar pneumonia, and commented that its rarity is curious when one recalls how rich is the blood during pneumonia in the elements necessary for coagulation. He said that he regarded venous thrombosis as a sequel rather than as a complication, the majority of cases occurring during convalescence.

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5. Lewis, Dean: Spontaneous Gangrene of the Extremities, Arch. Surg. **15:** 613 (Oct.) 1927.

6. von Winuvarter, F.: Ueber eine eigentümliche Form von Endarteritis und Endophlebitis mit Gangrän des Fusses, Arch. f. klin. Chir. **23:**202, 1878.

7. Meleney, F. L., and Miller, G. G.: Thrombo-Angiitis Obliterans, Ann. Surg. **81:**976 (May) 1925.

8. Austrian, Charles R.: Acute Lobar Pneumonia, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1921, vol. 3.

Goodhart,[9] describing symmetrical gangrene as a result of vasomotor or trophic neurosis, spoke of its association, among other conditions, with epilepsy.

Raynaud described the condition as being independent of all demonstrable anatomic changes in the vascular system, and stated that angiospasm alone caused the lesion. In view of later knowledge, angiospasm may be the result of local arterial lesion. Buerger stated that diseases due to vasomotor disturbances are the outcome of irritative and exhaustive processes of the sympathetic nervous system.

Isaac-Georges [10] reported two cases of his own in which the coincidence of beginning Raynaud's syndrome and influenzal pulmonary congestion was striking.

Adson and Brown [11] mentioned the close association of temperature and vasomotor changes with spasm.

SUMMARY

A fulminating, destructive symmetrical gangrene occurred in an epileptic girl, 7 years of age, with an acute respiratory infection after she was suddenly exposed, incompletely clothed, to zero temperature.

Any one of these conditions might be expected to conduce to neurovascular changes. That there was increased temporary coagulability of the blood of both legs in association with the respiratory infection may be presumed. The final result was thrombosis of the arteries and veins with inflammatory infiltration around the vessels.

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9. Goodhart, S. Philip: Vasomotor and Trophic Neurosis, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1921, vol. 10, p. 625.

10. Isaac-Georges, P.: Deux cas de syndrome de Raynaud apparus a la suite de congestion pulmonaire grippale, Bull. et mém. Soc. méd. d. hôp. de Paris **51**:1423 (Nov. 3) 1927.

11. Adson, A. W., and Brown, G. E.: Raynaud's Disease of Upper Extremities; Successful Treatment by Resection of Sympathetic Cervicothoracic and Second Thoracic Ganglions and Intervening Trunk, J. A. M. A. **92**:444 (Feb. 9) 1929.

DIPHTHEROID BACILLUS AS THE CAUSE OF ACUTE ENDOCARDITIS

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The organisms known as diphtheroid or pseudodiphtheritic bacilli form a loose ubiquitous group, and, owing to the inadequacy of present knowledge, one must still be conservative in regarding them as etiologic factors in the various diseases with which they are associated. Their relationship to the diphtheria bacillus is also unsettled. A number of observers [1] have maintained that all the diphtheria-like bacilli, including the solidly staining types such as Bacillus hoffmanni, are variations of the same species, the differences in morphology, cultural characteristics and pathogenicity depending on environmental conditions. Others [2] have included as diphtheroid bacilli those organisms that are identical with the Klebs-Loeffler bacillus in every respect except that they are nontoxic. This group has also been considered as an attenuated variety of the diphtheria bacillus which has lost its power of producing toxin.[3]

That B. diphtheriae is not always restricted to the mucous membranes was noted by Loeffler [4] himself, and since then much evidence [5] has been advanced that it often, if not regularly, enters the blood stream. It is surprising, therefore, that it so rarely gives rise to a general sepsis,

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From the Abraham Jacobi Division for Children and the Achelis Laboratory of the Lenox Hill Hospital.

1. Westbrook, F. F.; Wilson, L. B., and McDaniel: Varieties of Bacillus Diphtheriae, Tr. A. Am. Physicians **15**:198, 1900.

2. Wright, J. H.: Studies in the Pathology of Diphtheria, Boston M. & S. J. **131**:357, 1894.

3. Park, W. H.; Williams, A. W., and Krumwiede, C.: Pathogenic Micro-Organisms, ed. 9, Philadelphia, Lea & Febiger, 1929, p. 383.

4. Loeffler, F.: Untersuchungen über die Bedeutung der Mikroorganismen für die Entstehung der Diphtherie beim Menschen, bei der Taube und beim Kalbe, Mitt. a. d. k. Gsndthsamte **2**:440, 1884.

5. Conradi, H., and Bierast: Ueber Absonderung von Diphtheriekeimen durch den Harn, München. med. Wchnschr. **38**:1580, 1912. Jacobsthal, E.: Diskussion. Sechste Tagung d. Fr. Ver. f. Mikrobiol., Centralbl. f. Bakt. (Abt. 1) **54**:65, 1912. von Niessen: Diphtheriebacillen im Blute und in Behring'schen Heilserum, Wien. med. Wchnschr. **52**:2221 and 2283, 1902. Beyer, W.: Diphtheriebazillen im Harn, München. med. Wchnschr. **60**:240, 1913.

although frequently enough opening an avenue for secondary invaders, especially the streptococcus. If one leaves out of consideration the isolation of the diphtheria bacillus from the various organs or the heart's blood at autopsy, which may be a terminal invasion, in most of the cases reported as cases of diphtheria septicemia the bacillus is either associated with another organism, usually the streptococcus, or the isolated bacillus is nonpathogenic for the guinea-pig.[6]

An organism classified as a diphtheroid bacillus has been considered as the etiologic agent in a few cases of general sepsis,[7] and we could find but six cases in the literature in which it has been considered as the cause of acute endocarditis. Only three of these cases are acceptable. The case presented by Babes and Manolescu [8] was not one of pure diphtheroid endocarditis, as other organisms were found in the vegetations. In the cases reported by Hesse [9] and by MacLeod and Klaer,[10] the bacillus was cultured from the blood, but no autopsy was performed. Other organisms may have been present in the vegetations. In the remaining three cases the diphtheroid bacillus was the only organism isolated at autopsy in two (Howard,[11] Herzog [12]) and both from the blood stream during life and at autopsy in one (Roosen-Runge [13]). In view of the extreme rarity of the condition, it may well be, as Maixner [14] contends, that a diligent search would reveal that it is a mixed infection.

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6. Mahler, P.: Ueber einem Fall von Diphtheriebazillen und Streptokokkensepsin, Berl. klin. Wchnschr. **44**:1499, 1907. Ucke, A.: Ein Fall von Diphtheriebazillen-Septikämie, Centralbl. f. Bakt. **46**: 292, 1908. Leede, W.: Ztschr. f. Hyg. u. Infektionskr. **70**:104, 1911. Morgan, E.: Diphtheria Septicemia with Report of a Case, Am. J. Dis. Child. **5**:317 (April) 1913.

7. Francioni, C.: Sepsis aus diphtherieähnlichen Bazillus bei einem Säuglinge mit klinischen Erscheinungen winckelscher Krankheit, Monatschr. f. Kinderh. **7**:717, 1908. DeWitt, L.: A Case of Generalized Infection with a Diphtheroid Organism, J. Infect. Dis. **10**:36, 1912. Kessel, L., and Romanoff, A.: General Infection with a Diphtheroid Bacillus Complicated by Diphtheroid Meningitis, J. A. M. A. **94**:1647 (May 24) 1930.

8. Babes, V., and Manolescu, D.: Ueber einen in endocarditischen Exkrescenzen gefunden pseudo-diphtherischen Bacillus, Berl. klin. Wchnschr. **46**:67, 1909.

9. Hesse, F.: Diphtheriebazillen als Sepsiserreger, Deutsche med. Wchnschr. **35**:1096, 1909.

10. MacLeod, G. I., and Klaer, F. H.: Pseudodiphtheritic Septicemia with Report of a Case Diagnosticated by Blood Culture, Univ. Pennsylvania M. Bull. **21**:352, 1908-1909.

11. Howard, W. T.: Acute Ulcerative Endocarditis Due to the Bacillus Diphtheriae, Bull. Johns Hopkins Hosp. **4**:32, 1893.

12. Herzog, G.: Demonstration einer ulzerosen Endokarditis durch Diphtheriebazillen, München. med. Wchnschr. **65**:29, 1918.

13. Roosen-Runge: Ein Fall von Diphtheriebazillensepsin, München. med. Wchnschr. **50**:1252, 1903.

14. Maixner, E.: Endocarditis maligna ulcerosa, Ztschr. f. klin. Med. **75**: 143, 1912.

We have recently observed a case of acute endocarditis in which a diphtheroid bacillus was cultured from the blood both during life and at autopsy, and we are reporting the case because of the rarity of the condition and its inherent interest.

REPORT OF CASE

History.—V. N., a girl, aged 11 years, was admitted to the hospital on Dec. 30, 1930. She had had measles at the age of 6. One year prior to admission she had had pains in the right knee and fever for one week. Two weeks before admission she was taken suddenly ill, with a temperature of 102 F., malaise and loss of appetite. A diagnosis of grip was made. She gradually improved until December 25, when she was practically normal. The following day she had a relapse. She complained of pains in her back, left knee and abdomen. The pains lasted for one day. She then became irrational, and had been so since that time.

Examination.—Physical examination revealed an acutely ill, delirious white girl with a complete left hemiplegia. There was drooping of the left eyelid. The left pupil was widely dilated, but responded slightly to a bright light. The right pupil was normal. There were paralysis of the facial muscles on the left side and a deviation of the tongue to the left. There was marked rigidity of the neck, and the occiput was retracted backward to the left. The abdominal reflexes were absent on the left side and normal on the right. The left achilles tendon reflex was barely elicited. The left plantar reflexes were absent. A bilateral Kernig sign was found, and was more marked on the right side. A loud blowing systolic murmur was present, which was heard best at the apex and was transmitted to the left. The temperature was 101.8 F., and the pulse rate 98.

Diagnosis.—A diagnosis of acute meningococcic meningitis complicating a chronic cardiac valvular disease was made.

Course.—A spinal puncture was done, and 25 cc. of turbid fluid was withdrawn under marked pressure. Antimeningococcic serum was immediately injected.

The patient's general condition gradually improved and she became more rational, but the hemiplegia and the nuchal rigidity were still present. Ten days after admission a marked urticarial rash developed due to the serum injected. This disappeared in a short time. On the same day a tender area about half the size of a dime on the ball of the right toe was observed on palpation. A few days later several small, distinct, tender nodules were found on the right palm, right leg and right sole. There was marked tenderness of some of the cervical vertebrae. The patient's general condition, however, showed marked improvement, and she was quite rational although at times incontinent. On January 19, a few distinct petechiae were seen on the neck and one on the left eyelid. These daily became more numerous. On Jan. 24, 1931, examination of the eyegrounds showed a bilateral neuritis. On January 25, the patient became irrational again, and her condition grew steadily worse. On January 31, it was found that the left leg was cyanotic, cold and edematous. In addition there was a large decubitus ulcer over the left hip about the size of a half dollar. Small gangrenous areas developed on the left leg and the dorsum of the left foot and in two areas over the left heel. On February 3, the patient died.

She had had an irregular septic temperature ranging from 100 to 104 F. The spinal fluid on admission showed the following: white blood cells, 3,530; polymorphonuclears, 90 per cent; lymphocytes, 10 per cent; reducing substances,

0.54 mg. per hundred cubic centimeters; globulin, 4; chlorides, 0.64 mg. per hundred cubic centimeters, and pressure, 2+.

The abnormal conditions in the spinal fluid gradually cleared up, so that by January 13 the cell count showed but 27 white blood cells. Repeated smears and cultures for organisms were consistently negative. Successive blood cultures taken on December 30 and 31 and January 1, 6, 13, 16, 19 and 26 were negative. The cultures taken on January 27 and February 1 showed a diphtheroid organism. The blood count was 24,000 white blood cells, with 76 per cent polymorphonuclears and 24 per cent lymphocytes. The Wassermann and Pirquet tests were both negative. Chemical examination of the blood three days before death showed: urea nitrogen, 45.4 mg. per hundred cubic centimeters; creatinine, 2.1 mg.; uric acid, 4 mg.; sugar, 144 mg.; carbon dioxide combining power, 50 per cent by volume.

Frequent examinations of the urine showed occasional traces of albumin until January 28, when the albumin was markedly increased and microscopic examination showed many white blood cells and a moderate number of hyaline casts.

Autopsy.—The body was that of an emaciated white girl, 11 years of age and 135 cm. in length. There were marked pallor of the skin and visible mucous membranes. Numerous petechiae were present in the right conjunctiva and over the neck and thorax. Purplish gangrenous areas, measuring 5 cm. in diameter, were visible over both knees and the dorsal surface of the left foot and ankle. The left pupil was larger than the right.

The right pleural cavity contained about 25 cc. of slightly turbid fluid. Both lungs were lightly adherent to the parietal pleura by a fibrinous exudate over both lower lobes. The right lung weighed 300 Gm. and the left 250 Gm. The lower lobes of both lungs were dark red and firmer than normal and on section exhibited scattered dark red, raised, granular patches.

The pericardial sac contained no excess of fluid. The heart was lightly adherent to the pericardium over its posterior aspect and was markedly enlarged, weighing 350 Gm. On the anterior surface of the left ventricle were several old epicardial plaques. The posterior surfaces of both ventricles were covered with a thin fibrinous exudate. The right ventricle was markedly hypertrophied and dilated. Both auricles and the left ventricle were dilated and only moderately hypertrophied. The mitral orifice admitted but one finger. The mitral cusps were thickened, shortened and adherent. The chordae tendineae were thickened and shortened. On the auricular surface of each cusp adjacent to the free edge was a rather firm, grayish-pink vegetation, the size of a cherry nut. A few small verrucae were present along the overhanging free edges of the cusps. The endocardium of the left auricle was thickened. The aortic valve showed thickening of the free edges of the cusps and of the corpora arantii. The tricuspid valve was normal, except for dilatation of the ring. The pulmonary valve was normal. The heart muscle was yellowish brown and friable. Many of the muscular branches of the left coronary artery were apparently plugged with an opaque grayish-yellow material, and the heart muscle in their immediate vicinity was necrotic and hemorrhagic. The aorta was grossly normal.

The spleen was much enlarged; it weighed 275 Gm., and was lightly adherent to the under surface of the diaphragm, the under surface of the left lobe of the liver and the surrounding structures. The surface of the spleen revealed many large and small, elevated, sharply demarcated, yellowish areas. On section, these areas were opaque, yellow and firm. At the lower pole was a purplish, soft, cystic area the size of a plum which was filled with yellowish fluid and necrotic material. The pulp was soft and semidiffluent and exhibited many small, white miliary spots.

The liver was much enlarged, weighing 1,150 Gm. It was yellowish brown, and on section had a "nutmeg" appearance. Scattered through the organ were several small, grayish miliary spots, and near the capsule, covering the anterior surface of the right lobe, were several larger yellowish nodules, one of which was apparently calcified.

The right kidney weighed 110 Gm., and the left 90 Gm. Both were enlarged and grayish white. The capsules stripped easily, exposing many sharply demarcated, grayish-white areas. On section these areas were wedge-shaped and opaque yellow. The cortical markings were indistinct, and scattered small miliary spots were visible.

The stomach, intestines, pancreas and suprarenals exhibited no gross abnormalities.

The bladder was filled with purulent urine, and the mucosa was congested and hemorrhagic.

At the bifurcation of the abdominal aorta and extending for a short distance into both common iliac arteries was a friable, adherent, grayish-pink thrombus, 0.8 by 1.4 cm. A dark red, propagated thrombus completely filled the lumina of the vessels beyond this point. A bluish mass measuring 3 by 5 by 2 cm. was situated at the bifurcation of the right common iliac artery. It was filled with a friable thrombus. The continuity of the arterial wall was lost at this dilatation, and both the external and the internal iliac arteries emptied into it.

Microscopic Examination: The heart muscle exhibited fibrinopurulent pericarditis and extensive diffuse purulent infiltration of the interstitial tissue with the formation of multiple small abscesses. Numerous septic thrombi were found occluding the coronary vessels and surrounded by necrotic, hemorrhagic and purulent areas. The muscle fibers showed intense degeneration, as was evidenced by cloudy swelling, fatty degeneration, vacuolization and finally complete necrosis. Several small mural thrombi were present, which in one area showed early organization. Marked congestion and edema and moderate intrafascicular fibrosis were also present. No Aschoff bodies could be demonstrated. The mitral valve was the seat of an acute valvulitis with extensive infiltration of polymorphonuclear leukocytes. The vegetations were composed of platelets and fibrin with no endothelial covering and showed masses of bacteria in the superficial layers.

The lungs showed congestion edema, desquamation of the alveolar cells and numerous "heart failure cells" loaded with pigment. There were scattered areas of atelectasis and a patchy bronchopneumonia. Occasionally, the alveolar walls in the pneumonic areas were necrotic.

The liver showed congestion, fatty degeneration of the parenchymatous cells and diffuse polymorphonuclear infiltration. Beneath the capsule were several miliary abscesses.

The spleen exhibited intense acute splenitis with multiple septic infarcts.

The kidneys showed suppurative nephritis. There were numerous septic infarcts and small abscesses besides a diffuse polymorphonuclear infiltration. The cells lining Bowman's space were swollen and occasionally desquamated. Many of the glomerular tufts were collapsed while others were adherent to the capsule. The loops exhibited swelling of the endothelial lining cells, vacuolization, fibrinoid and hyaline thrombi, increase in the number of nuclei, polymorphonuclear infiltration and occasionally masses of bacteria. Many of the glomeruli were surrounded by an acute inflammatory exudate, and an occasional polymorphonuclear cell was found in Bowman's space. The tubular epithelium was undergoing severe degenerative changes, and many of the lumina contained casts and polymorphonuclear leukocytes. There were marked edema, congestion and many small hemorrhages.

Anatomic Diagnosis.—The anatomic diagnosis was: acute bacterial endocarditis of the mitral valve, chronic endocarditis of the mitral and aortic valves, acute fibrinopurulent pericarditis, acute suppurative myocarditis (embolic), chronic interstitial myocarditis, cardiac hypertrophy and dilatation, acute serofibrinous pleuritis, bronchopneumonia, chronic passive congestion of the lungs and liver, fatty degeneration of the liver, acute suppurative hepatitis, acute splenitis and perisplenitis, multiple septic infarcts of the spleen, acute suppurative nephritis (embolic), acute cystitis, riding embolus of the bifurcation of the abdominal aorta, mycotic aneurysm of the right common iliac artery, early gangrene of both lower extremities and petechial eruption.

Bacteriology.—The organism isolated from the blood had the characteristics of Corynebacterium hoffmanni. It occurred as gram-positive, nonmotile, short plump rods and stained unevenly with alkaline methylene blue. No metachromatic granules or polar bodies could be demonstrated. The organism was cultivated without difficulty on ordinary mediums at 37 C. On plain agar and blood agar it formed discrete, homogeneous, smooth, pearly gray colonies with entire edges. After forty-eight hours on the latter medium, methemoglobin was produced. The same organism was isolated in cultures from the heart's blood at autopsy. Smears made from the vegetations, however, revealed that besides numerous diphtheroid bacilli, scattered gram-positive cocci were present. These occurred singly or in pairs. The vegetations were not cultured, as the specimen had already been placed in formaldehyde.

COMMENT

Clinically and pathologically the case reported was one of acute vegetative endocarditis of the mitral valve, complicated by widespread embolic phenomena. The interesting feature was the isolation of a pure culture of a diphtheroid bacillus from the blood stream seven and two days before death, and from the heart's blood at autopsy. Repeated blood cultures up to that time had yielded negative results. We were, therefore, greatly surprised when smears of the vegetations showed the presence of a streptococcus in association with the diphtheroid bacillus. That in a small number of cases of acute endocarditis, usually estimated at 10 per cent, the streptococcus cannot be recovered from the blood stream is well known. Besides these considerations, the extreme rarity, if not altogether doubtful existence, of a diphtheroid endocarditis makes it highly probable that the streptococcus was the etiologic organism in our case and the diphtheroid bacillus a secondary invader.

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PEPTIC ULCERS IN CHILDREN

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Peptic ulcer is a common malady among civilized races, no age seemingly being immune. In infancy and childhood this disease is comparatively uncommon. The rarity of peptic ulcer in childhood is probably more apparent than real, as many cases are not recognized during life and others not until adult life. The diagnosis of peptic ulcer in childhood is in the same position as the diagnosis of such a condition in adults was about twenty-five years ago; only cases with the more common complications are recognized. A correct diagnosis in the uncomplicated cases is but rarely made. Palmer [1] collected reports of forty-five cases of chronic peptic ulcer in childhood; in only ten cases was a correct clinical diagnosis made. Rogers [2] stated that at present the majority of peptic ulcers in children are diagnosed post mortem. In many cases the condition is wrongly diagnosed as chronic appendicitis, pylorospasm, cyclic vomiting, intestinal indigestion, etc.

The diagnosis of peptic ulcer in childhood is not made with sufficient frequency, for the following reasons: 1. Ulcer is not suspected in childhood. 2. In younger children a history cannot be obtained. 3. Uncomplicated cases do not give a history typical of ulcer. 4. Roentgen examinations of the digestive tract in childhood are not made with the same frequency as in adults.

Ulcers of the stomach and duodenum may be of various types and causes. In this paper, however, I shall discuss exclusively the chronic peptic ulcer. As to the etiology, I shall refer the reader to the extensive discussions on this subject in standard textbooks and current literature. Suffice it here to say that, presumably, the etiology of chronic peptic ulcers in children is the same as that of the disease in adults, namely, at present, uncertain.

The diagnosis is based on the history, physical examination and roentgen evidence. A history of chronic digestive disturbances, anorexia, night pain and vomiting is suggestive of a peptic ulcer. A history of hematemesis or melena is very suggestive. Occult blood in the stools is also suggestive of an ulcer. The visualization by a roentgen examina-

1. Palmer, D. W.: Duodenal Ulcer in Infancy, Ann. Surg. **73**:545, 1921.

2. Rogers, J. S. Y.: Duodenal Ulcers in Two Infants of the Same Family, Arch. Dis. Child. **3**:163 (June) 1928.

tion of a filling defect characteristic of an ulcer either in the stomach or in the duodenum is diagnostic of this condition.

In recent years three cases of peptic ulcer in children were observed by me, and I shall record them briefly.

REPORT OF CASES

CASE 1.—A. D., a boy, aged 12 years, was first seen in May, 1928. He gave the following history. He had had indefinite digestive disturbances for from five to six years, characterized by abdominal distress and frequent pain in the mid-epigastrium and the right lower quadrant. There was no food relationship, but the pain frequently wakened him from sleep. There was belching and heartburn, but no vomiting. His appetite was poor, and he was somewhat undernourished. There was marked constipation, relief from which required frequent catharsis. Two years previously, following a roentgen examination, the condition was diagnosed chronic appendicitis. Soon afterward, an appendectomy was done. The appendix was reported as chronically inflamed. There was no relief from the symptoms after operation. In May, 1928, he was again examined by the roentgen rays. At this time a penetrating ulcer of the lesser curvature was demonstrated. The physical examination gave entirely negative results. Examination of the stomach contents showed normal acidity, but there was a faintly positive guaiac test for blood. Repeated examinations of the stools when the patient was on a meat-free and fish-free diet showed occult blood to be present.

A diagnosis of gastric ulcer was made. The patient was placed on a modified Sippy [3] diet, and the symptoms promptly subsided. Six weeks later, at reexamination after a barium meal, the niche on the lesser curvature of the stomach was definitely smaller. Another roentgen examination of the stomach in January, 1929, revealed no trace of the deformity. The patient has remained symptom-free, except for a very mild recurrence for about one week in July, 1930.

CASE 2.—H. R., a boy, aged 10 years, was first seen on April 15, 1930. His illness had begun twenty-three months before. The onset was acute, with cramp-like pain in the abdomen and vomiting. The vomitus contained some blood. The following day he passed a tarry stool, and appeared pale. The abdominal pain persisted, occurring chiefly between 1 and 2 a. m., when the patient would awaken. Occasionally, this pain was accompanied by vomiting, but the vomitus never again contained blood. Vomiting gave relief from the pain. The bowels were costive. At that time, he was closely observed and question of a cerebral tumor was raised. After careful investigation, however, nothing confirming this was discovered. A

3. The Sippy regimen consists of rest in bed, frequent feedings and thorough neutralization of the stomach contents. The treatment begins with hourly feedings of equal portions of milk and 20 per cent cream, twelve such meals being given during the day. Alkalis in the form of sodium bicarbonate, calcium carbonate and magnesium oxide are given hourly between meals. To this basic food are gradually added cooked cereals, eggs, toast, butter, gruels and later minced chicken, meat, fish and purée of vegetables and fruits, so that at the end of three weeks the patient is getting three simple meals daily, with supplemental feedings of milk or milk and cream between meals. At the same time, the number of alkaline powders is diminished to three or six daily.

gastro-intestinal roentgen examination disclosed a deformity of the duodenum. A tentative diagnosis of duodenal ulcer was made. For the next fifteen months the patient was entirely symptom-free, and during this remission he gained 28 pounds (12.7 Kg.). Three weeks prior to the first consultation, the patient suddenly wakened about 2 a. m. with epigastric pain. The pain recurred nightly up to the time he was first seen. He vomited almost every night, bringing up 1 or more quarts of sour-tasting material which contained neither blood nor old food. There was distinct relief after the administration of sodium bicarbonate. He lost 4 pounds (1.8 Kg.) during the three weeks.

Physical examination gave entirely negative results. Examination of the contents of the stomach showed normal acidity. The stools, examined repeatedly, showed no occult blood. Roentgen examination showed a persistent irregularity of the duodenum without any six hour gastric residue.

On a Sippy diet with frequent ingestion of alkalis between meals, the patient remained symptom-free and gained 10 pounds (4.5 Kg.) within the last year.

CASE 3.—R. P., a girl, aged 12 years, was first seen on May 8, 1930. For seven months, the patient had had more or less persistent epigastric pain, more marked from one to two hours after meals. There was no night pain. There was considerable belching and heartburn. At no time did the patient vomit. She abstained from food for fear of pain following a meal. She lost 8 pounds (3.6 Kg.). Under the advice of her family physician she took calcium carbonate, which relieved her from pain somewhat. The bowels had moved daily, but the calcium caused her to become constipated. The first week in May she spent in bed in an attempt to obtain relief from pain. During the same time she was placed on a modified Sippy diet, with considerable relief.

Physical examination gave negative results, except for enlargement of the tonsils. The roentgen examination showed a prepyloric ulcer with a 30 per cent six hour gastric residue. With a further modified dietetic regimen, tincture of belladonna and alkalis, the patient became symptom-free and remained so for six months. Her present condition is not known to me.

COMMENT

Treatment for peptic ulcer in childhood is similar to that for the condition in adults. The children are fortunately not exposed to some of the gastric irritants, such as tobacco, alcohol, etc. Foci of infection, particularly tonsillitis, are common in children, and must be eradicated if the best results are to be obtained. However, a word of warning is not amiss. The removal of healthy tonsils, no matter how hypertrophied, will not help in the control of the symptoms of ulcer; the removal of diseased tonsils, *per se,* will not cure patients with ulcers. The appendix is sometimes removed as a possible focus of infection. It does not seem justifiable to expose a child to a major surgical procedure in the hope of eliminating a focus of infection which in the individual case may have nothing to do with the presence of the ulcer.

The treatment for uncomplicated ulcers is medical. The dietetic regimen must be adjusted to the age of the patient. Fortunately, the

simple foods according to either Sippy's or Lenharz'[4] diets are well suited to children. The greater importance of vitamins in the diets of infants and children must be borne in mind. No child should be kept on a diet without vitamin C for more than six weeks. The prevention of deficiency diseases is an important part of the medical regimen. The results of medical treatment for uncomplicated ulcers are fully as good in children as in adults. Patients with ulcer having hemorrhage are a more serious problem, as children do not stand the loss of blood as well as adults. Transfusion of blood must be considered in every case in which a considerable hemorrhage has occurred and in which the red blood count and hemoglobin examination reveal serious loss of blood.

Perforation of an ulcer requires immediate surgical treatment. The mortality is very great. Palmer[1] reported a successful pyloroplasty and a later gastro-enterostomy in a boy 6 months old. Weber[5] reported two cases of successful gastro-enterostomy, with relief from symptoms, in children, 12 and 15 years of age, respectively. Patients with peptic ulcer complicated by partial pyloric obstruction are best treated medically; only when the patient is not relieved is surgical intervention indicated.

CONCLUSIONS

1. Peptic ulcers in children are more common than is generally realized. Many cases are clinically overlooked.

2. Peptic ulcers should be suspected in a child with chronic digestive disturbances not explained by any other demonstrable pathologic process.

3. The finding of occult blood in the stools is suggestive of a peptic ulcer.

4. A roentgen examination of the digestive tract demonstrating a typical deformity is the only means of arriving at a definite clinical diagnosis of peptic ulcer.

5. The treatment for uncomplicated peptic ulcer is medical.

6. Complications in cases of peptic ulcers must be treated accordingly, perforations requiring immediate operation, and hemorrhage and a partial pyloric obstruction being treated medically by choice and surgically from necessity only.

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4. The Lenhartz diet consists of eggs and milk for about one week. At the end of the first week, sugar, rice, zwieback or toast and butter are added. Later, meat and mashed vegetables are allowed. The patient is fed in small amounts, hourly at first, then every two hours at the end of ten days. Complete rest in bed is insisted on.

5. Weber, M.: Zur Kasuistik des Ulcus ventriculi im Kindesalter, Arch. f. klin. Chir. **137**:731, 1925.

Progress in Pediatrics

PSYCHIATRIC WORK WITH CHILDREN

SOME PRESENT-DAY TRENDS

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One of the outstanding movements in the field of public health during the past decade has been the application of the principles of dynamic psychiatry to the problems revolving around the development of the child. In this field psychiatry is having its widest social opportunity to promote mental health and to create and disseminate through our complex civilization a better appreciation of how personalities are shaped—the things which motivate the variety of behavior responses, normal and abnormal—and to develop a better appreciation of the essentials for healthy human relationships in home, school, industry and other phases of normal life.

This field has developed with great rapidity and at times has been associated with impulsive and unwise enthusiasms. It has opened some hope in the field of mental disorder, where hopelessness has usually been the dominant note; when some light is cast on a rather dark field, certain distortions are bound to follow, and some false hopes are created. This happened to some extent when the child was discovered as the golden opportunity for mental hygiene. These enthusiasms were inevitable and at times were followed by some deflation of interest, but they should not be allowed to prejudice any thoughtful person against the real values that modern psychiatry and other disciplines are contributing to a better understanding of the large problems revolving around the mental development of the child.

Out of clinical experience in these fields there is gradually emerging a point of view about behavior, both for children and adults, that is sound and therapeutically applicable. There is developing an appreciation that mental phenomena (behavior) are understandable as scientific facts with a genetic background which, if understood, shows why behavior problems develop in the first place and the purpose the prob-

From the Philadelphia Child Guidance Clinic.

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lem behavior serves as it continues. This point is best illustrated by the following situation: A 14 year old boy gives a history of many years of rebellion against various forms of authority, resulting in his expulsion from several schools. He was the only boy of parents who were poorly adjusted to each other; they separated, and the boy lived with the mother and her family. To the mother this boy always was identified with two difficult things in her life, which prevented a normal relationship between mother and son: he represented all the unhappiness associated with her marriage; he was identified with all the difficult traits possessed by the father. Every time he showed any difficult behavior the fear was aroused that he would be like the father, and as he grew he showed more and more reactions of a rebellious, overassertive type. Efforts to eradicate the behavior were severe and continuous, and the rebellion of the boy against this began early and continued. He had no secure place in the love life of his home, and as a result he had little opportunity to gain any sense of his own values. In the group he became overassertive, because he was shy and afraid of being called yellow. His rebellious behavior came to have two values to him: 1. It had the effect of drawing attention to him. 2. It served as a method of punishing his mother for her treatment of him. These values have continued. This boy's behavior becomes understandable in terms of his own background and relationships. Treatment, to be effective, must bear a close relationship to the things that have kept the turmoil going.

Psychiatric work with children, which always will include a great deal of adult work, is giving clear indication of the need of working with all the facts, regardless of the particular field in which they are found—constitutional, nutritional, endocrine and other physical facts—psychogenic, etc. Psychiatry can advance only with that broad philosophy and background which seek to work with the facts wherever they are found and regardless of the school of thought that has contributed to the better appreciation of what these facts mean in terms of human experience. Distortions in understanding behavior will always occur when the subject is approached with fixed attitudes and with prejudices against certain things. Whenever the point of view is myopic, important things will be overlooked. For example, an adolescent boy presented certain explosive behavior reactions. The parents had been told that unless a certain type of endocrine medication was given, the boy would become a dangerous criminal, although there was nothing at the time in his behavior that warranted such a gloomy forecast. The one fact of a somewhat indefinite endocrine disturbance led to a neglect of many other important things in the boy's background and relationships and led to a disturbing and destructive

piece of advice being given. This will happen when behavior is approached with a prejudiced and solidified point of view.

Certainly the trends in this field indicate that there is no discrepancy between the so-called organic and the psychogenic approach to behavior. Both approaches reveal facts that are necessary for a balanced understanding of the case, and yet violent disagreements have taken place between the adherents of both schools, leading at times to infantile demonstrations rather than to a calm and scientific desire to know the true meaning of the facts and how they have contributed to a behavior disturbance. Common sense should show the importance of both and that no real discrepancy exists.

If thorough physical examinations fail to reveal important pathologic processes, it is unscientific to go on thinking that if one had more refined methods one might find the cause of the trouble in this field. Such a point of view is based on prejudice against psychogenic phenomena. It is not scientific to take minor physical difficulties and to pin one's entire therapeutic hopes on their correction, important though the correction may be. Even in the presence of major physical disorders it must be recognized that other things may have to be accomplished when these conditions have received their proper attention.

It is true that one of the important trends in psychiatry, particularly as it is applied to children, has been in the direction of attaching more importance to the various life experiences and relationships of the child, particularly of those in the family group. This wide field includes many psychogenic factors challenging better understanding and capacity to deal with them. The assignment of proper values to these psychogenic factors has been partially blocked by a fear that such things are outside the sphere of scientific investigation. A question commonly asked is, "How can you prove the connection between such things as a parental attitude toward a child and the child's behavior?" Usually such questions are followed by the statement that they are not susceptible to experimental proof, and they cannot be duplicated in a test situation. This is quite true; but does that fact eliminate a scientific attitude toward social phenomena and the attachment of objective values to the things that people say and do and think about themselves and each other? The trend has certainly been in the direction of attaching a scientific validity not only to the facts themselves, but to one's capacity to study and treat these facts.

Psychiatric work with children has taken the physician into a broad field of human activity which has extended far beyond the confines of abnormality and diseased conditions. It has been concerned with knowing the child as a unit within himself, with an emotional life and a physical organism peculiarly his own. His behavior responses are seen as the external expressions of attempts to bring about a har-

monious and satisfying adjustment to a variety of situations. The child himself must be understood for what he is and for what he seems capable of being. While the child is an individual, he is also a social being and cannot be dissociated from his setting. He influences and is influenced by things happening around and to him. The realization of this has led to a real appreciation of the dynamics of family life and the emotional problems that each individual brings to it. Work with children, therefore, has emphasized the importance of knowing parents as well as children and of appreciating the things that have formed their own background and influenced the attitudes that they have, not only toward their children but toward their own adult situations. The understanding of the emotional background of the home has become one of the important objectives in children's work. Interest still attaches to the grosser and more tangible things of the social setting, which in the past have absorbed most of the attention in endeavors to understand behavior. One has looked at the condition of the house, the food and the neighborhood and a variety of other things that make up the more tangible environment of the child; while the importance of these things is still recognized and is not to be minimized, the newer trends have focused on understanding the people who live in the house. This changing point of emphasis has broadened the field under discussion more than any other single thing.

There is also the large field that concerns the understanding of the child as he goes into the community, as he steps beyond the dependency of his home life into the life of the school, playground, church, etc. As one result the whole field of children's psychiatry has become related closely to the educational methods and resources of a community and has helped to make schools and other community resources more conscious of the needs of the individual child.

Several important things have developed as a result of the broad contacts made necessary by this wider field of activity. Probably the most important contribution has come from an appreciation that several professional groups have a mutual field in which to operate and in which they can pool and coordinate their efforts. The field of mental hygiene, which includes the one under discussion, has extended far beyond the strictly medical field. It is important that physicians recognize this in order that due appreciation may be attached to the professional contributions of the educator, the social case worker, the psychologist and other professional groups.

Cooperation between these groups has not always proceeded in a harmonious way. Jealousies still exist, and statements are made regarding the intrusion of one group into a field belonging to another, etc. A recent meeting in a nearby city was called to determine the type of leadership that should be given to a new clinic. Some of the professional

groups represented spent much of their time discussing the inadequacies of the others in order to show their own priority. This point of view has not been an uncommon one and has blocked many important developments in psychiatric work with children.

My own feeling is that leadership in the clinical field must rest with the well rounded, adequately trained social psychiatrist, but leadership does not mean domination and an assumption of medical superiority. Leadership in this field requires the recognition of, and capacity to utilize, contributions of the other important professional groups and not merely to see them as aids to carry out the orders and advice of the psychiatrist. Mental health and happiness are the goals to be achieved in a mental hygiene program, and the educator, social case worker, personnel worker in industry, the minister and others have just as real a part in the achievement of this goal as has the physician.

Psychiatry has profited a great deal by these contacts and at the same time is making a real contribution to the philosophy of these other groups. As a result, we find more and more social workers, teachers, psychologists and sociologists thinking of behavior in somewhat the same terms. A common language and point of view are essentials of cooperation. Mutual contacts are helping to bring this about, with the result that all are gaining a better understanding of human behavior and the factors that motivate the reactions of people and shape the early personalities of children.

The emphasis on the broad understanding of the child and his relations has made increasingly apparent the futility of classifications that are dogmatic and frequently misleading. Formal classification has had a stunting influence on adult psychiatry by focusing more attention on the symptom than on the dynamics of the symptom. The breadth of the children's field has made impossible any extensive scheme of formal classification and the use of terms suggestive of definite entities. Children with neurotic symptoms, with educational disabilities, with tendencies to delinquency and with a variety of personality difficulties indicative of a faulty adjustment are constantly presented to every child guidance clinic. Attention has been focused on the continual question of why is this behavior going on in this person? Labels give a false sense of having reached some decision, whereas too frequently they cover the fact that nothing has been understood. Take the favorite term "constitutional psychopath" or any of its numerous variations. It attempts to describe an entity, but really conveys no understanding as to what is happening in the life of a person so designated. Usually it conveys a pessimistic feeling that nothing can be understood. A truer appreciation of the meaning of behavior observed in such persons is obtained when one studies them as one would study any other human being with an interest in understanding the kind of a person he is and

the things that seem important in shaping his present responses. Thus the trend in the children's field has been to use diagnostic labels very sparingly.

Psychiatric work with children is giving a clearer understanding of the normal needs for healthy mental growth. Some of the more obvious factors have long been understood and sometimes accepted as the whole story. The need for a healthy body, sensible habit training in the necessities of daily routine, good food, fresh air, suitable recreation, intelligent educational opportunities and harmonious homes are generally accepted as important. But as this work has progressed there has been developed a clearer appreciation of some of the more subtle and frequently more important factors. Of particular importance is a better understanding of the parent-child relation and the things determining its healthy and unhealthy aspects. A child's most fundamental need is to feel secure in his own home, to feel that he is respected and wanted, not for what he can satisfy in the emotional life of his parents, but for his own individual self. This security provides the base from which the child gains the courage to grow and to assume gradually the responsibility that growth brings. Growth involves giving up things and replacing one form of pleasure for another; frequently it is a painful process. A child's capacity to handle anxiety arising from the incompatible feelings of love and hate and to stand the give and take of competition are but a few of the things requiring courage from a child. This courage can emerge only from a secure base which the child gains in his early years. A clearer conception is being acquired of the things that interfere or help in the establishment of this base. The more mature and well adjusted the parents, the more natural will be the development of a secure place for the child. Parents commonly carry into their relationship with their children many unresolved conflicts of their own. A father struggling along from the effects of a deprived love life in his own childhood or a mother clinging to a strong attachment to her own parents are instances of problems found in the emotional lives of parents which frequently enmesh the child. These things do not always stand out on the surface. They operate in homes that give the surface indication of normality, and that would satisfy the more conventional standard of a good home. An understanding of these more subtle things helps to clear up some of the puzzling questions that are commonly asked when a behavior problem emerges in a home that seems to be perfectly normal.

Some of the more important trends revolve around the questions of treatment. It is one thing to know the factors that create a behavior problem in a child; it is another and a far more difficult matter to deal with these questions in a constructive and helpful way.

The principles of physical treatment in this field are no different from those in any other field of medicine. Good medical judgment indicates the need for a sound physical condition, the attainment of which should be one goal of every program of treatment. In this paper, therefore, my discussion will be on a consideration of the phases of treatment that are less well understood and that concern the understanding and modification of attitudes and emotional conflicts.

One of the earlier things that impressed the workers in this field was the marked futility of the approach that emphasized such negative attitudes as blame, lecturing, telling people what to do, etc. These approaches usually aroused antagonisms and resistances, and blocked the way to the development of a relationship between the therapeutist and the patient which helped in the understanding of the factors underlying the difficulties. If one blames what has already been done, one inhibits the bringing up of other things that have been going on and that have had an important relation to the emergence of the acts that are condemned. The individual may even seek condemnation as a means of protecting himself against the discussion of more basic difficulties. Healy's comments on stealing as a cloak to a conflict over sex is an interesting illustration of this.

Treatment that is primarily directed toward the behavior and its eradication is as unsound as medical treatment that would center attention on the removal of pain and fever. Such a program of treatment, now uncommon in clinical medicine, but still common in the field of behavior disorders, disregards the factors underlying and causing these symptoms to emerge.

Psychiatric treatment for children has passed through several stages. Earlier methods were largely manipulative, with attention focused on such things as changing schools, providing better recreation and healthier outlets for activity, relieving bad economic situations and giving better habit training. Certain favorite placebos used to be: "Send the child to a military school." "Send the child to the country." "Take him out of school because he is nervous." Such advice is still given rather commonly and is based on a feeling that something must be done, so try this and see what happens. A great deal of specific advice was given as to child management during this period. This manipulative type of treatment has its place and when used with judgment helps certain types of problems. This approach requires less time and less understanding of more complicated situations, and becomes wofully insufficient only when more serious difficulties must be treated.

The trend in treatment has been away from this authoritative type of approach, which consisted largely in assuming a responsibility that normally belongs to the individual. In doing this the therapeutist takes away from the patient a sense of his own capacity to deal with the problems

of his own life. Instead of reducing confidence, treatment should result in restoring a type of self-confidence that will enable the individual to deal with his own situations without creating problems. An interesting case illustrates this point. A case was studied of a young child whom the mother said she could not manage because of his severe outbursts of temper. She wanted the child placed, as that offered the most immediate relief for the problem. First the child was placed in a day nursery with the mother caring for the child at night, but the problem continued, and then the mother insisted on more radical placement, and the child was sent to a foster home. The feeling all along was that these were purely palliative steps which only accentuated the mother's sense of her own inadequacy against which she was struggling. As the child improved somewhat in the foster home, the mother insisted on having the child back. These steps had done nothing to relieve the problem, but, having gone through them, the worker began to feel the need of knowing this mother somewhat better and helping her to talk about her own difficulties and to understand why she felt so inadequate to deal with this child. The emphasis in treatment shifted from the giving of specific advice and moving the child from home to home to the building up of a relationship with the mother which enabled her to get a better understanding of what was going on within herself. Through this relation the worker was able to give the mother a different feeling about herself, which, in turn, enabled her to accept in a more adequate way the responsibilities that superficially she had been attempting to dodge. Treatment in this case became effective only when manipulation was stopped and emphasis was placed on helping the mother to understand some of her own problems, which were preventing a healthy relation with the child.

Trends in treatment have been in the direction of emphasizing the therapeutic possibilities of the relationship established between the therapeutist and patient. This is important both for child and adult and offers a chance for the patient to understand the things within himself that have contributed to the formation of a problem. This is different from using the relationship of telling people what to do and what not to do. The creation of this constructive relationship requires a capacity to take every situation that is presented and try to undertsand it just as it is—not as one would ideally like to have it. This means that an approach is made with an open mind and one which does not congeal the persons seeking help. Many parents and children present behavior that commonly stirs up prejudice and condemnation. This is true with the brutal father, the promiscuous mother and the child with sex difficulties. If therapy is to be effective, such persons must have a feeling that at the outset they are accepted for what they are, and that there is an interest in understanding them at that level as a start to helping them to adopt patterns of behavior more in keeping with healthy living.

This relationship should allow a person to feel that he is accepted uncritically, that he has an opportunity to drop off many of his defenses, and that he can describe and discuss the way he actually feels about things that are difficult to face and that he will avoid if possible. Even though the therapeutic relationship does not extend beyond one or two interviews, something constructive is introduced into a case when it is given this tone. Psychiatrists are not detectives and are not interested in the cross-examination of patients merely to get facts. One may drag a lot of facts from a patient during an interview and be unable to do anything with them after one has them. Facts will follow when a good relationship is established, and when they come they will begin to have meaning, because the patient has been able to discuss them spontaneously. For example, a boy of 14 was involved in some sex difficulty at school. He was referred to the clinic by a physician who saw the need of doing more than merely preventing a recurrence of the particular act. From the beginning it was clear that it was going to be difficult for this boy to talk about these difficulties, and it would have been destructive if the psychiatrist had attempted to force such discussion. It would have been just as bad if he had been so protective of the boy that he had told him that he knew all about the difficulties, thus relieving the boy of the necessity of talking about a difficult subject. Later the boy will discuss these and other important things, and when he does the facts will have much more meaning to him than if they had been forced out prematurely or if he had been confronted with them. It is easy to lose the cooperation of the patient by stressing a single point of behavior. That happens when too much emphasis is placed at the beginning on merely getting a person to tell what he has done.

SUMMARY

In this paper I have tried to combine a consideration of certain trends in the broad general field together with certain trends in the specific technics that have been evolved to deal with the clinical problems presented. In closing, I will reemphasize one or two points.

It is clear that in order to meet the health needs of children there must be more understanding of the emotional and personality problems associated with child development. The realization of this has opened a field of clinical activity that has brought psychiatry in touch with the broad problems of human relationships, particularly those revolving around family life. If psychiatry is to make a lasting contribution in these broad fields, two important considerations must be incorporated into the thinking of medical people and other professional groups concerned with human behavior.

1. Clinical programs must advance on a broad base that has an interest in working with all the facts influencing human behavior, with-

out prejudice and without crystalized ideas as to what is important and what is nonessential. The development of this critical judgment is one of the needs of present-day psychiatry; without it there can be no progress in harmonizing the conflicting points of view that grow from a one-sided vision of behavior.

2. The second point follows from the first. When the physician and others have achieved some of the cardinal human virtues of tolerance, patience and curiosity, there will be more appreciation of the fact that behavior must be understood before there can be treatment for it. Mere cessation does not mean correction. A child who has been stealing may be stopped from stealing and may still present as serious a problem as before. A real appreciation of this point, when incorporated into psychiatric practice, into schools, courts, social agencies, family life and even into the broad philosophy about how human beings develop and change, will do a great deal toward giving a constructive and scientific approach to the problems of human behavior.

AN EARLY UNDERTAKING IN HOSPITAL SOCIAL SERVICE

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Social service in the hospitals of this country is a comparatively recent development. Fifty years ago even the beginning of such a service did not exist, while today no hospital that makes a pretense of being a modern institution is without the beginning of such a service, and in some instances forty or fifty paid social workers are employed for the needs of a single hospital. Unpaid volunteer workers have always been associated with the paid workers in the better hospitals, and perhaps their service represents nearly as large a service to the community as that rendered by the paid worker.

It has seemed wise to review briefly the factors and to study the growth of so epochal a movement in the modern community health program. For the sake of historical accuracy, if for no other reason, it should be studied in order that credit may properly be given the originators of a movement that has a unique place in the modern renaissance of medicine.

The inception of social service into the modern hospital lay in the effort to retain individualism in medicine. With the growth of dispensaries and hospitals, an unmanageable increase occurred in the number of patients treated by the physician. It was not long before the physician discovered that often a diagnosis could not be completed without some knowledge of the social background of the patient, and that the treatment was usually wholly inadequate unless he could extend his influence beyond the boundaries of an institution. Formerly, the family physician followed the lives of his patients as friends, and through many years watched the growth and development of families. Hence he was supposed to have an understanding of family and individual constitutions; thus he was popularly credited with having special advantages over a newcomer, even though it was generally granted that the stranger had a better education and even greater natural gifts of

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Read before the Section of Historical and Cultural Medicine of the New York Academy of Medicine, Jan. 13, 1932.

mind. In any event, the family physician touched the lives of his fellows on many sides and when he came to their aid in his narrower professional capacity he could supplement his diagnostic findings and his therapeutic resources with a wealth of knowledge which years of association with them outside of the sick room had furnished him. It was perhaps natural that the lack of outside contact with the family should first be felt in an infant's hospital and that the necessity for such a communication should manifest itself early as a paramount need in such an institution.

The first hospital in the city of New York given over entirely and exclusively to the care and study of infantile diseases as separate from those of the mother was opened in 1883 by Dr. Sarah McNutt in the old Post-Graduate Hospital.[1] The work gradually expanded so that after a few years a remodeled dwelling house was entirely occupied by the babies' wards. With the building of a new hospital, a separate unit was given to the babies' wards, so that by 1894 the Post-Graduate Hospital had one of the best equipped plants in the world for the care of sick infants. In these wards many of the basic principles which have since become commonplaces in the hospitalization of children were first stated as rules of conduct. From the beginning of the babies' ward it was demanded that: "The hygienic surroundings must be of the best, the nursing of a high grade and the most scrupulous and painstaking oversight exercised," [1] and furthermore, that "one good nurse should be supplied to not more than four or five sick infants, and in many cases one nurse was required for only two patients." [1]

Shortly, however, it was noted that a large number of patients were returned to the wards after discharge, suffering from a renewal of the same illness. In order to make permanent the benefits of the hospital [2] Dr. Henry Dwight Chapin, in 1890, made an appeal to a committee of women for aid in visiting children discharged from the hospital. In response to this appeal a small voluntary group began to study the circumstances of patients discharged from the hospital so that proper aid could be given when required. Though amateurs in hospital social work, these visitors had had training in social case work in other fields of social endeavor. Furthermore, they followed closely a plan, worked out from 1890 to 1892, in which a study of six hundred cases was made to discover the social conditions of the families of infants admitted to the wards; it was concluded that: "Causes as well as the cure, must be

1. Chapin, H. D.: The Babies' Wards of the New York Post-Graduate Hospital, Arch. Pediat. **14**:328 (May) 1897.

2. Chapin, H. D.: The Work of the Babies' Wards of the New York Post-Graduate Hospital for Convalescent Children, Arch. Pediat. **22**:241 (April) 1905.

individual and social."[3] When they visited the home of a patient, they filled out a blank covering not only the address and age of the parents but additional data such as number of rooms, the amount of light and air in the apartment, the sanitary condition of the house and street, the economic and physical condition of the parents, and the intelligence exercised in the care of the children in the home. Two weeks after the child's return home, a visit was made to determine the progress that was being made toward health by the child since its discharge from the hospital. Four years later (1894) it became evident that a regular paid visitor was required, and accordingly a woman physician was appointed to carry on the undertaking. After a fair trial, it was found that a nurse, with an instinct for social service work, did better under the circumstances than a physician as "it may be that the latter emphasized the purely medical aspect of the work, which is not the main feature in this undertaking."[4] In a paper published by Dr. Chapin in April, 1905,[2] the same year in which Dr. Richard C. Cabot established his first paid worker at the Massachusetts General Hospital, a study of the social record of a thousand cases covering a period of from March, 1900 to March, 1902, was made. While it was realized that "hospital statistics, as such, are of little value unless they take into consideration the ultimate condition of the patient,"[2] it was nevertheless pointed out that: "Until hospital managers are able or willing to extend their work along these lines of permanency or have agencies that will do so, their work fails in much of its possibilities."[2] In 1917, Dr. Chapin summarized the hospital social service effort, covering by this time a period of twenty-three years, as follows:

> A combination of hygienic knowledge, tactful sympathy and good power of observation and judgment are required in this kind of work. In addition to a study of conditions, a human personal touch must always be maintained. Our aim is to have the endeavors of the visitor expended in three principal directions: (1) To try and make the medical relief given by the hospital to the individual as permanent as possible. This may mean immediate material relief in cases of necessity or instruction in diet and other factors that may be required to further convalescence. (2) To find out, if possible, the underlying cause that produced the particular sickness so that a recurrence can be prevented. (3) To make a broad study of social conditions that make for sickness and disability in the community that is served by the hospital. The latter becomes necessary in order that a general knowedge in reference to future prevention may be acquired and constantly kept in mind.[4]

It is interesting to learn something of the details of the investigation and of the reports turned in by the social workers, which included

3. Chapin, Henry Dwight: Child Study in the Hospital: A Record of Six Hundred Cases, Forum **17**:125, 1894.

4. Chapin, H. D.: Hospital Social Service for Children, M. Rec. **91**:353 (March 3) 1917.

the period beginning in 1891. The following points were studied and reported on in detail: From the beginning, the economic life of the patients was stressed, it being realized that this was not only a matter of income, but, aside from the clothes and the food, of housing. It was observed whether the home and its surroundings were hygienic, whether it was as inexpensive as could be obtained with due consideration of health, decency and distance from work, friends and amusements, and whether it was large enough to safeguard the decencies of family life. Questions were asked to find out if there were roomers or boarders (and if so, how many) and, so far as possible to discover the state of health of the family. At an early stage it was realized that one cannot generalize in many of these matters as the customs and previous habits are important: one race or one set of people may have so adjusted themselves as to preserve the decencies of life under conditions impossible for another.[5] Thus the social worker not only reported on the religion and race of those investigated, but was also expected to note the intelligence of the family and to report her conclusions as to whether it was a suitable home, all things being considered, for a convalescent infant. In a word, she attempted and often succeeded in these early years of hospital social service in making the hospital record not only an interesting, but above all, a true human document.

In these early years, the social service worker was intrusted with a small sum of money to relieve immediate distress, but from the beginning this was closely guarded, not because it was difficult to obtain, but to avoid dependence.[6] In this manner, in the ten years preceding 1905, the procedures and principles that are today the commonplaces of hospital social service were gradually built.

A further step was obviously necessary as the result of this social service experience. It was soon apparent that many homes were not suitable for convalescence because of ignorance, poverty, lack of equipment or many other circumstances which originally lead to the removal of the child to the hospital. The first attempt to solve this problem was in the establishment of an institution for convalescent infants on the north shore of Long Island.[2] In a few years it was realized by Dr. Chapin that this was no answer to the question, as infants and small children, even more than adults, need individualism, not only in their rearing, but in their physical care, and that, furthermore, of no little importance was the fact that the risk of cross infection was still present. Thus began the attempt to place children temporarily in proper homes under the care of a competent physician and a visiting trained nurse or

5. Chapin, H. D.: Work for Convalescent Children, Hosp. Soc. Serv. **1**:114 (May) 1919.

6. Chapin, H. D.: The Relation Between the Child and Hospital Social Service, J. A. M. A. **77**:279 (July 23) 1921.

nurses. This step obviously carried forward to its logical conclusion the social service experience at the hospital. This effort has become so successful that it has been organized and incorporated into what has become known as the Speedwell Society.[2]

It will be noted that hospital social service was not only established but that its main principles were formulated and published in various short papers by Dr. Chapin during a period of ten years beginning with 1891. Dr. Richardson,[6] in the Children's Hospital of San Francisco, saw the folly of giving people medicine without knowing their living conditions, and, as early as 1886, appointed a nurse to visit homes to give instructions in cooking and in hygiene, to supply extra diets when needed and to interest individuals to contribute to needy cases. There were, however, no records kept other than those required for financial book-keeping. It remained for Dr. Chapin to appreciate the great service which a social service worker could render to the patients in the hospital. In this undertaking from 1891 to 1916, three thousand seven hundred cases were studied at different periods and under varying economic conditions in an endeavor to make, in a cross-section, a social diagnosis of the illnesses. From these studies it was concluded that the causes could be traced back to three general categories, namely, "insufficient earnings, bad housing and ignorance on the part of the parents." [6]

At an early date it was appreciated that this meant that the efficiency and earning capacity of many persons must be increased; the overcrowding and unhygienic housing must be overcome somehow, and that a wide campaign of health education must be carried on in the community served by the hospital. The success of this social service experience which was so quietly begun in the New York Post-Graduate Hospital in 1891 under the direction of Dr. Chapin is perhaps best measured not by its spread in the course of forty years to other hospitals but by the efforts which have been made to improve the community life and the better chance given the infant of growing up into a normal adult. It has helped to make the hospital a broad human institution, and as has so often happened in this world a child has led the way. Hospital social service, like many other endeavors to improve social conditions, had its beginning in pediatrics.

Pediatric Biographies

JACOB RUEFF

1500–1558

JOHN RUHRÄH, M.D.
BALTIMORE

Rueff's name was variously written Ruff, Rüff, Ruoff and Ryff, and he should not be confused with Walter Reiff, who plagiarized Rösslin. Born in the Rheintal in 1500, he is noted as living in Zurich in 1525, where he acquired a reputation as a *"Steinschnyder."* He was a physician, surgeon, author and preacher all combined, and was well thought of by his contemporaries. Conrad Gesner refers to him as "Vir in arte sua peritissimus," most skilled in his art. Apart from his medical writings, he wrote verse and several plays, including a couple of comedies and a play based on the story of Wilhelm Tell. After the manner of his day, he dabbled in astronomy and astrology. In 1532, he was made *Stadtarzt* in Zurich. He died in 1558.

His medical writings include: "Ein schön lustig Tröstbüchle von den empfengnussen und geburten der menschen, und jren vilfaltigen zufälen und verhindernussen, mit vil und mancheiley bewärter stucken und arznyen, auch schönen figuren, darzu dienstlich, zu trost allen gebürenden frouwen, und eigentichem bericht der Hebammen, erst nülich zusammen geläsen durch Jacob Rüff, Burger und steinschnyder der loblichen Statt Zürych. Getrucht zu Zürych bei Christoffel Troschouer, 1554."

This book was reprinted in 1559, and again by Sigm-Feyerabendt in 1580. It was subsequently reprinted in 1588 and 1600. Latin editions appeared in 1554, 1580 and 1587, and, according to Haller, there was a Dutch edition dated, Amsterdam, 1670. He also wrote "Libellus tumoribus quibusdom phlegmaticis non naturalibus, Tiguri, 1556." This was reprinted in Amsterdam in 1662. Eloy states that this book on tumors is more valuable than his contribution to obstetrics.

His obstetric book was based largely on Rösslin, but he added his own points of view, and it is really his own book. He advocated correcting the position of the child by external manipulation and other obstetric procedures. He figures 32 plates of monsters and should be regarded as the father of teratology, even if some of his plates are

fantasies borrowed from the past, such as a child with an elephant's head and one with wings and bird's feet copied from older writers.

The later editions of the book contain directions for the care of the new-born. The edition of 1580 is entitled: "Hebammen Buch. Daraus man alle Heimlichkeit des Weiblichen Geschlechts erlehrnen Welcherley gestalt der Mensch in Mutter Leib empfangen Zunimpt und geboren

Von wartung der Neuwgebornen Kinder. 245
Ein vnderweisung wie sich die Schwangern Frauwen halten sollen.

In Reimen verfaßt.

DJe schwangern Frauwen solln zuuorn
Vor grossem schrecken vnd vor zorn
Sich allzeit hüten sonderlich/
Für vnmut auch bewaren sich.
Zur Adern keine lassen sol/
Die not erheisch dasselb dann wol.
Es wer denn vmb die zeit vnd stundt/
Daß sie in vierdten Monat kompt.

Hh iij Auch

Beginning of the rhymed part of Jacob Rueff's 'Hebammen-Buch," 1580.

wirdt. Auch wie man allerley Krankheit die sich leichtlich mit der kinderbetterin zutragen mit Köstlicher artzeney vorkommen und helfen Könne. Alles aus eygentlicher Erfahrung dess weitberümpten Jacob Ruffen Stattarzts zu Zurich viz dieser Zeit an Tag geben. Jetzund aber von newen gebessert mit schönen Figuren geziert sampt einen mutzlichen Anhang von Cur und Pflegung der neu-gebornen Kinder. Gedruck zu Franckfort-am-Mayn-MDLXXX." (The Midwives Book. In which all the secrets of the feminine sex are taught; how the form

of man is received in the mother's body, grows and is born. Also how all kinds of diseases easily happen in child-bearing and how they may be helped by costly medicines. All presented from the personal experiences of the world renowned Jacob Ruffen, physician of Zurich. Now newly improved with beautiful plates and including a useful appendix on the cure and care of new-born children. Printed in Frankfort-on-Main—1580.)

This is the sprightliest of the poems dealing with child care that I have found, and while the subject matter does not differ much from the other books of the period, the presentation has much charm.

Recent writers have stressed exercise as part of the regimen of the young infant. The idea is not new as will be seen by the following selection:

So lang baden, bis dass sein leib
Ganz rotlicht wirdt, dan ist es zeit,
Dass du es nimmest aus dem bad,
Jedoch so merck auch diesen rath.
Das Wasser sol nur lawlecht seyn,
Darnach salb es mit honig fein.
Nach dem so wasch ihm one laugen,
Die öhrlein sauber und die augen.
Trückne es dann mit tüchlein weiss,
Zuletzt soltu es auch es auch mitfleiss,
Mit Baumöl gar wol ersalben
An seinem Leibe allenthalben.
Dann soltu auch all seine glieder
Biegen, hin her, auff und nieder,
Die Bein, den Halz den Rück die Hendt,
Die Arm die Seiten und die Lend,
Nach dem sie sollen sein gestalt,
Solches bringt in nutzen manigtalt.
(Bathe only so long until his skin
Is reddened from the foot to chin,
When from the bath the babe you take,
This admonition must I make
The water, lukewarm, with honey fine
Anoint the child, then cleanse his ey'n
But here you must not be severe
And likewise wash each little ear.
With a white cloth the child you dry
And olive oil you then apply.
Then must you exercise each limb
Bending them up and down and in
The leg, the neck, the hands, the back,
The arm, the sides, the hip—no lack
The body's uses manifold.
By this process you help unfold.)

One or two other excerpts may be quoted in free translation which will give a further idea of the extent of the propaganda for child care in the sixteenth century:

How one should care for the new-born child
Of the young child and of its care
What it shall eat and drink and wear
Early and late, asleep, awake
We shall now learn what pains to take.
So tender a thing, of mother born
Needs special care, so let us warn
Roses and salt together pour
Sprinkle the child, behind, before,
Body and face and leg and arm
Which keeps the skin from hurt and harm
Or else lest cold and chafe should spoil
Anoint it well with acorn oil,
Which helps the skin and is not wrong
Strengthen the joints and makes them strong.
And then you cut the navel string
Four fingers broad and to it bring
Upon the end which you have cut
A powder made of Trachenblut
And Sarcocolla and pure myrrh.
And in some Roman kimmel stir
And bolus too and over all
Lay cotton dipped in olive oil
And bind the belly with a cloth
And after bathing always swathe
And keep it clean until at last
The cord falls off and danger's past.

. . . . . .

How the mother should suckle and feed the child
When children are not really well
Give milk foods for this little spell
And with the same the baby feed
Until the teeth begin to breed.
During this time give only milk
Nor any foods of other ilk
For they will make the child quite ill
And note this also if you will
No other milk must one suggest
Save what he sucks from mother's breast.

Pediatrics in Art

MULTIPLE ARTHRITIS

JOHN RUHRÄH, M.D.
BALTIMORE

Sandro Botticelli, more properly, Alessandro di Mariano dei Filipepi (1444-1510), figures in his Madonna and Child with the two Saint Johns, reproduced here, now in Berlin, a case of multiple arthritis in the

Madonna and Child with the Two Saint Johns

hands of the Child and also in those of the Virgin. The changes are most marked in the second joints. Changes are also seen in the fingers of the Child in the Madonna del Magnificat, while the Child in the Madonna del Melagrana shows one joint which could well be a tuberculous condition, although it may be due to the foreshortening in the drawing. The Madonna and the Child in the Poldo-Pezzoli Museum in Milan also shows joint changes, while none are noted in the Madonna and Child and St. John, the Mystic Nativity, Madonna and Child with Six Saints, Madonna and Child with Angel and Primavera. These may be studied in the Medici Society reproductions by Yokio Yashiro. The photograph here is by the Photographische Gesellschaft, Berlin.

News and Comment

GENERAL NEWS

The Report of the Encephalitis Committee in Holland.—In 1927, when encephalitis postvaccinalis occurred in alarming frequency in Holland, the law which decreed compulsory vaccination was temporarily not enforced, and a committee was appointed to study the cause of this complication and the ways to combat it. This committee has now published a report on its activities, which contains the whole story concerning encephalitis postvaccinalis. Several hypotheses have been investigated, but no solution for the problem has been found. The report is interesting in many respects, especially since different possibilities have been extensively examined and several facts revealed. There appears to exist no relation between the neurotropism for the vaccine used and the occurrence of complications in the brain. Encephalitis postvaccinalis occurred with all kinds of lymph; however, it occurred more frequently with one kind than with another, and it could not be discovered whether this was also related to other factors. Animal experiments to produce encephalitis postvaccinalis failed. In the discussion on the etiology two hypotheses are especially stressed (that the condition is due to the activation of a latent virus or that the vaccine virus itself causes the disease), but neither of them can be proved. As to the prophylaxis, one can partially rely on empiric information; it appears that encephalitis postvaccinalis occurs less frequently during the first and second year of life, and that when the children are older the frequency increases (1924-1927; in children from birth to 1 year, one case in 14,038 vaccinations; 1-2 years, one case in 32,865 cases and 1-11 years, one case in 1,879 vaccinations). The question remains undecided whether it is advisable to vaccinate. The number of cases of encephalitis postvaccinalis after revaccination is small (1929: one in 2,415 vaccinations and one in 51,333 revaccinations). Experience with the serum of persons vaccinated shortly before the illness is too limited to warrant definite judgment as to its therapeutic value.

Hospital Discontinues Undergraduate School.—The board of directors of the Children's Hospital, Washington, D. C., put into effect, April 1, a new plan which stops the admission of new students in its training school, and which accepts only graduate and affiliate students for nursing service. Students already in the school will be graduated on satisfactory completion of their course.

UNIVERSITY NEWS

Well Baby Clinic at the University of Indiana School of Medicine.—An anonymous gift of $5,500 to establish a well baby clinic at the University of Indiana School of Medicine has been announced. The clinic will be operated for three years once a week at the Coleman Hospital, in connection with the department of pediatrics.

Dr. W. McKim Marriott, dean and professor of pediatrics, Washington University School of Medicine, St. Louis, will be the lecturer at the University of California Medical School for 1932-1933.

The University of California Medical School announces the promotion of Dr. Francis S. Smyth to professor of pediatrics.

Dr. Ralph M. Tyson has been appointed professor of pediatrics at Temple University, Philadelphia.

At the annual commencement of the Medical College of the State of South Carolina, June 2, these faculty appointments were announced: Dr. Wythe M. Rhett, assistant professor of pediatrics; Dr. Joseph I. Waring, lecturer in pediatrics.

PERSONAL

The American Committee for the International Congress of Pediatrics, to meet in London, July, 1933, has elected Dr. H. F. Helmholz, Mayo Clinic, Rochester, Minn., chairman; and Dr. C. A. Aldrich, 723 Elm Street, Winnetka, Ill., secretary.

Abstracts from Current Literature

Anatomy and Physiology

THE REGRESSION OF THE DUCTUS BOTALLI IN MAN. A. COSTA, Cuore e circolaz. **14**:546, 1930.

The minute histologic structure of the duct and its involution have been investigated in sixty cases, including embryos in various stages and new-born infants. During fetal life the intima is thick and has little elastic tissue, the muscular cells being arranged lengthwise; it is rich in mucoid matter. The muscular wall proper has a circular inner layer and a longitudinal outer layer of muscle cells and contains elastic tissue and some mucoid matter. This type of structure should favor the discharge of the blood from the pulmonary artery to the aorta. After birth the lumen of the duct grows narrower because of an elastic hyperplasia of the muscular wall and of the internal elastic coat and the intima. The mucoid material diminishes. The anatomic closing is completed by the formation in the lumen of a blood clot with calcium and iron. This precipitation of minerals is followed by a fibrous elastic sclerosis of the walls of the duct with atrophy of the muscle cells. Chronologically, the processes differ in different places.

G. PATRASSI. [ARCH. PATH.]

THE AREA OF THE ORTHODIAGRAM OF THE HEART AS A MEASURE OF THE SIZE OF THE HEART IN CHILDREN. ADOLF FRANZ HECHT, Jahrb. f. Kinderh. **133**:26 (Sept.) 1931.

As an index of the size of the heart, Hecht takes 100 times the area of the cardiac shadow in square centimeters divided by the two-thirds power of the weight of the child in kilograms. (For instance, the size of the heart of a child weighing 27 Kg. is 63 sq. cm.; the two-thirds power of 27 is 9. The quotient would be $63 \div 9 = 7$. In order not to be obliged to work with decimals, the author multiples by 100, which would make the quotient 700). A large series of normal and pathologic cases is treated by adequate statistical methods. Children with a history of rheumatism, but without cardiac involvement, have small hearts. During growth, the heart becomes relatively smaller. After infections, it may be enlarged for as long a time as a year.

CLAUSEN, Rochester, N. Y.

Pathology, Bacteriology and Biochemistry

STUDIES ON THE PROPERTIES OF BOUILLON FILTRATES OF THE MENINGOCOCCUS: PRODUCTION OF A SOLUBLE TOXIN. N. S. FERRY, J. F. NORTON and A. H. STEELE, J. Immunol. **21**:293 (Oct.) 1931.

The authors describe experiments indicating the production of a soluble meningococcus exotoxin. The toxin is contained in the filtrate of a bouillon culture incubated for from four to six days. This toxin produces a positive cutaneous reaction in susceptible persons in as high a dilution as 1:1,500. It is antigenic, and a neutralizing antitoxin was produced in horses and rabbits. There is a specific toxin for each of the four Gordon types. The endotoxin obtained by mechanical disruption of the bacterial cells or by autolysis is not type-specific, but is common to all four types.

FOTHERGILL, Boston.

THE CORRELATION OF THE PROTECTIVE VALUE WITH THE TITERS OF OTHER ANTIBODIES IN TYPE 1 ANTIPNEUMOCOCCUS SERUM. LLOYD D. FELTON, J. Immunol. **21**:341 (Nov.) 1931.

Felton points out the desirability of having some accurate method for standardizing antipneumococcus serum. He points out the difficulties and errors inherent in the expensive mouse protection technic.

For this reason the correlation between protection and the various other immune reactions was studied. He found that for type 1 the correlation coefficient between protection and precipitin titer is 0.93; between protection and agglutination, 0.80; between protection and neutralization, 0.88, and between protection and the amount of protein precipitated with specific carbohydrate, 0.91. From his experiments on a large number of serums, he finds that accurate and reproducible results can be obtained by determining the amount of protein in the serum precipitable with the soluble specific substance.

FOTHERGILL, Boston.

THE USE OF ETHYL ALCOHOL AS PRECIPITANT IN THE CONCENTRATION OF ANTIPNEUMOCOCCUS SERUM. LLOYD D. FELTON, J. Immunol. **21**:357 (Nov.) 1931.

The protective substance in antipneumococcus serum is insoluble in from 15 to 20 per cent alcohol at 0 C. The inert, water-soluble material can be removed by washing, and the water-insoluble protein (which contains the protective substance) can be dissolved in a solution of salt. Alcohol as a precipitant yields at least 80 per cent of the protective substance found in the original serum. It is possible to dry the precipitated active material with retention of its immunologic characteristics.

FOTHERGILL, Boston.

THERMOREGULATION IN FOWL. ALEXANDRE GIAJA, Ann. de physiol. **7**:13, 1931.

The author makes an inclusive study of the mechanism of the regulation of heat in the goose, the cock and the turkey. In the goose and the cock regulation by loss of heat plays the important rôle; so that one finds in general only feeble variations in the production of heat for marked differences in the temperature of the surrounding atmosphere. In the turkey, which has a less heavy covering of feathers, regulation by the production of heat prevails over regulation by the loss of heat. These results were obtained by the respiration calorimeter, and were confirmed by measuring the food consumption of the fowl in question on a maintenance diet, at varying temperatures of the surrounding air.

Having determined the values at basal metabolism and the optimum metabolism, if one elevates the temperature of the surrounding air above the body temperature of the animal in question, thermolysis appears in the form of a thermal polypnea. When the polypnea is not accompanied by a hyperthermia, one proves that the loss of energy descends below the value of basal metabolism at the temperature limited by the appearance of the polypnea. Consequently, the basal metabolism, such as was actually determined, would not be the minimum of loss of energy of the homeotherm, but the loss that is accomplished when it fights neither against heat nor against cold, a state that most homeotherms instinctively try to realize.

The expenditure of energy of the plucked bird is greatly increased, and one does not succeed in returning the energy to the basal values of the normal bird by elevation of the temperature of the surrounding atmosphere. This increase in energy is relatively greater at low temperatures than at elevated temperatures, which would indicate that the plumage has a protecting power as great proportionately as the surrounding temperature is low. In studying the heat, or energy, saving protective power of the plumage, one finds that this power is stronger at low temperatures, and that it is modified only a little by intense currents of air. The plumage is a protective layer to which one cannot apply the simple laws of conductivity of heat. In the living bird, the plumage is not a passive covering, but an apparatus possessing the faculty of modifying considerably its heat-protecting power. It is with the aid of this apparatus that the birds studied, notably the goose, each regulate their loss of heat according to the needs of their homeothermy, in such a way that regulation by thermogenesis has not in them the importance that it has in the thermoregulation of the majority of mammals.

BUDSON, Ann Arbor, Mich.

THE FUNCTION OF THE ARTERIES AND VEINS IN MAN. TECHNIC OF REGISTERING BY MEANS OF ELECTRO-ANGIOGRAMS AND INTERPRETATION OF CURVES IN NORMAL SUBJECTS. ALDO LUISADA, Arch. d. mal. du cœur **24**:305 (May) 1931.

With a special type amplifier and a mirror galvanometer, Luisada has been able to register the electrical phenomena of arteries in living animals. He has carried out similar studies in man, using several technics. The method that proved most suitable required the use of two hollow nickle needles enclosed in a thin layer of celluloid. Each needle at the base ends in a mouth piece of ebonite to which is fitted an ebonite cone containing a cotton pledget. The needles are filled with physiologic solution of sodium chloride, and the cones, the cotton of which is also saturated with the same solution, are fitted on. The skin is pierced at the desired spot; then the cones are pressed in a manner to cause a small drop of liquid to leave the points of the needles under the skin. A connection is made to the cotton in the cones with a nonpolarizable Du Bois-Reymond electrode, and the wire of this is attached to the amplifier. By placing the two needles in such a manner that the points are a distance of 1 cm. apart, perpendicular to the artery and very close to it, a good conduction is effected by the liquid path. In this way, such phenomena are excluded as polarization currents, skin currents and phenomena due to distention of the tissues at the arrival of the flow of blood. Muscular currents are very slight if the patient remains quiet in the horizontal position; if he moves, they are easily recognized, as they are from ten to twenty times greater than the others.

The same method can be used for the veins. A pneumatic cuff is used to distend the vein, and the two needle points are brought to rest in the wall of the vein itself.

Several arteries were studied—the femoral, radial, dorsalis pedis and brachial. The author describes the form and relations of the curves obtained, and discusses their nature. He also makes some interesting deductions regarding the physiology and pathology of the circulation.

The article is well illustrated with diagrammatic sketches and reproductions of the curves that the author obtained in this study. TURNER, Chicago.

THE MECHANISM OF RED BLOOD CELL SEDIMENTATION; COMPARATIVE STUDY OF THE INFLUENCE OF THE FORMED ELEMENTS OF THE BLOOD, THE COLLOIDS, CERTAIN CRYSTALLOIDS AND THE ALKALINE RESERVE. C. ACHARD, A. CODOUNIS and E. HADJIGEORGES, Arch. d. mal. du cœur **24**: 657 (Nov.) 1931.

During studies of blood sedimentation, the authors, using the same patients, have made parallel studies of the influence of the number of erythrocytes and their hemoglobin content, the influence of the leukocytes, the action of the osmotic pressure of serum proteins and the relative levels of these proteins (serine and globulin), and the influence of fibrinogen, assuming that the speed of sedimentation is, above all, a plasma reaction. At the same time they have studied the lipoid equilibrium, certain crystalloids, plasma chloride, total nonprotein nitrogen, and finally, the variations of the alkaline reserve.

They conclude that the elements that may influence the sedimentation of erythrocytes are first the different fractions of plasma proteins, also the red blood cells and their hemoglobin content, and then the amount of nitrogen loss and modifications of the acid-base equilibrium. The influence of lipoid equilibrium seems to be nil and that of plasma chloride very uncertain. TURNER, Chicago.

THE DETERMINATION OF THE OXYGEN CONTENT IN SMALL AMOUNTS OF BLOOD. H. W. MOOK, Nederl. tijdschr. v. geneesk. **75**:4049 (Aug. 1) 1931.

The author describes a method of determining the oxygen content of a small amount of blood. He uses the same apparatus as formerly described for the

determination of the "alkali reserve." He also describes the method by which the blood must be taken from the finger in order not to let it come into contact with the air, so that the oxygen content and the degree of saturation of the capillary blood can be accurately determined. For this purpose he uses small tubes (length, 35 mm.; internal diameter, 3 mm.; content, about 250 c.mm.).

VAN CREVELD, Amsterdam, Holland.

PHOSPHATASE IN THE YOUNG AND IN THE FETUS OF RABBITS. ISOO HORII, MASAMICHI MORII and ENRYO NARIOKA, Arb. a. d. anat. Inst. d. kaiserl. Univ., Kyoto, 1931, series C, no. 2, p. 37.

The authors found that there was no difference in the phosphatase action of the organs of the body in 45 and 30 day old rabbits, while in those just born the splitting possibilities were distinctly lower, and in the fetus the splitting possibilities were markedly lower.

SANFORD, Chicago.

Nutrition

COMPARATIVE DIETARY STUDIES OF AMERICAN CHILDREN OF NURSERY SCHOOL AGE. J. C. WINTERS, Am. J. Pub. Health **21**:1003 (Sept.) 1931.

The average daily protein intake in grams per kilogram of body weight is: Mexican boys, 2.39; Mexican girls, 2.40; Negro boys, 2.37; Negro girls, 2.45; American boys, 2.63, and American girls, 2.36. The average daily carbohydrate intake in grams per kilogram of body weight is: Mexican boys, 71.14; Mexican girls, 66.75; Negro boys, 80.16; Negro girls, 72.49; American boys, 77.60, and American girls, 72.54. The average daily calcium intake of Mexican boys is 0.5731 Gm.; of Mexican girls, 0.5191 Gm.; of Negro boys, 0.5819 Gm.; of Negro girls, 0.5657 Gm.; of American boys, 0.9172 Gm., and of American girls, 0.7714 Gm. The average phosphorus intake of Mexican boys is 0.8801 Gm.; of Mexican girls, 0.9001 Gm.; of Negro boys, 0.8031 Gm.; of Negro girls, 0.7189 Gm.; of American boys, 0.9768 Gm., and of American girls, 0.8155 Gm. The average daily iron intake of Mexican boys is 0.00555 Gm.; of Mexican girls, 0.00468 Gm.; of Negro boys, 0.00706 Gm.; of Negro girls, 0.00662 Gm.; of American boys, 0.00702 Gm., and of American girls, 0.00613 Gm.

KUGELMASS, New York.

HYPERVITAMINOSIS D AND ARTERIOSCLEROSIS. H. L. VANDERVEER, Arch. Path. **12**:941 (Dec.) 1931.

For this study twenty-four healthy young rabbits were used, ranging in age from 3 months to 1 year. Viosterol with a vitamin D potency 10,000 times that of good cod liver oil was used. It was given subcutaneously twice a week; the dosage for the 1 year old rabbits was 0.5 cc. per kilogram and the dosage for the younger rabbits was varied proportionately. The termination of each experiment was the spontaneous death of the animal. Microscopic and macroscopic studies of the autopsy material were made. The arterial sclerosis produced was not of a specific type for vitamin D, but resembled that produced by epinephrine hydrochloride, barium chloride and digitalin. The earliest calcareous deposits in the blood vessels were found to be an incrustation about the elastic fibers of the media. Degeneration of the muscle cells appeared later. Other tissues showing calcareous deposits were the kidneys, stomach, heart, liver and lungs, apparently degeneration of tissue due to a toxic process precedes calcification of the organs. No changes were found in the bone marrow or in the parathyroid glands comparable to those formed in hyperparathyroidism.

LESLIE, Evanston, Ill.

THERMOPHILIC MICRO-ORGANISMS FROM IMPORTED CANNED SHALLOTS (ONIONS). PAUL S. PRICKETT, J. Infect. Dis. **49**:271 (Oct.) 1931.

The author analyzed 379 cans of Italian shallots for the presence of toxins or viable toxin-forming bacilli. Only 84 cans were sterile. Fifty-eight contained

the toxin or spores of Clostridium botulinum, and the remainder such organisms as were frequently isolated from canned foods in this country and types totally inocuous when fed to healthy guinea-pigs. TOOMEY, Cleveland.

MATERNAL NURSING AND THE DENTAL SYSTEM. CORRADO D'ALISE, M. J. & Rec. **124**:95 (Dec. 16) 1931.

Deficient constitution and structure of the first permanent molar and the incisors are due fundamentally to maternal or artificial nursing that is insufficient in quality. Pathogenic and embryogenic studies of teeth give a valid contribution to the knowledge of the physiopathology of lactation. It is a good practice to furnish stale whole grain bread to the mother during pregnancy and nursing and to the baby after weaning in the form of pap. Apart from other advantages, maternal nursing contributes to the normal development of the dental arches, the hard palate, the nasal fossae and the other structures of the head and, indirectly, to the development of the whole body. WILLIAMSON, New Orleans.

HOW CHILDREN GROW. RUTH SAWTELL WALLIS, University of Illinois Studies, series 208, vol. 5, August, 1931.

An anthropometric study of private school children from 2 to 8 years of age is reported. This study includes body measurements, roentgenograms and data on dentition. A full bibliography is included. SANFORD, Chicago.

PERMEABILITY OF THE HEMATO-ENCEPHALIC BARRIER FOR AROMATIC SUBSTANCES IN ACUTE NUTRITIONAL DISTURBANCES OF INFANCY. S. SCHAFERSTEIN and S. P. PERSITZ, Jahrb. f. Kinderh. **132**:194 (July) 1931.

The chemical methods used are not stated; however, no evidence was obtained that "aromatic bodies" are increased in the cerebrospinal fluid in toxicosis.

CLAUSEN, Rochester, N. Y.

THE RÔLE OF THE HEMATO-ENCEPHALIC BARRIER IN THE ORIGIN OF THE NEUROTOXIC SYNDROME IN ACUTE NUTRITIONAL DISTURBANCES: IV. ACETONE BODIES. S. J. SCHAFERSTEIN, Jahrb. f. Kinderh. **133**:75 (Sept.) 1931.

In cases of the "neurotoxic syndrome" the author observed an increase in the ratio between acetone bodies in the cerebrospinal fluid and in the blood; he believes that this demonstrates an increased permeability and accounts in part for the symptoms. CLAUSEN, Rochester, N. Y.

INFLUENCE OF MINUTE AMOUNTS OF PHOSPHORUS ON THE GROWING BONES. M. OKUMURA, J. Pediat. (Tokyo), Nov. 20, 1931, no. 378, p. 1573.

The author administered (by injection) from 0.15 to 0.01 mg. of elementary phosphorus in olive oil to young rabbits and rats, according to the body weight. The injections were made daily for a period of from two to six weeks. The body weight was found to be much less in the treated animals than in normal controls. The length of the long bones was also less than in the normal controls. Histologically, the ossification process at the epiphyses of the long bones showed a process of decreased absorption rather than of acceleration. These results seem to differ from those obtained by other workers. No explanation is offered.

KATO, Chicago.

RICKETS IN JAPAN. S. IZUMI, J. Pediat. (Tokyo), Nov. 20, 1931, no. 378, p. 1606.

The author presents the clinical aspects of rickets in Japan in great detail, with the aid of forty-eight tables containing careful observations. His conclusions

are: 1. The disease is most prevalent in the districts fronting the sea, but it is also fairly well distributed throughout the land. 2. The fact that hemoglobin values are decreased in rickets is not necessarily characteristic of this disease, and the same may be said of the appearance of basophilic stippling of the erythrocytes. 3. The amount of inorganic phosphorus and calcium in the blood serum is usually low in rickets, but the diagnosis of rickets may be made when the values are high in the presence of clinical symptoms. 4. The serum phosphatase in rickets was thought to have a peculiarly characteristic significance in diagnosis, but the results of experiments seem to prove otherwise. 5. There was no marked acidosis in rachitic patients who were carefully studied. 6. There is no difference in the main symptoms and the characteristic roentgenograms between the Japanese type and the European type. 7. There seems to be no single symptom or test that is solely characteristic of rickets, and the correct diagnosis must depend on the total picture of the disease.

KATO, Chicago.

Prenatal Conditions

CONGENITAL HEART DISEASE: A CLINICAL AND PATHOLOGICAL STUDY OF TWO CASES OF TRUNCUS SOLITARIUS AORTICUS (PULMONARY ATRESIA). M. A. KEEGEL, Am. Heart J. **7**:263 (Dec.) 1931.

This is a clinical and pathologic study of two cases of truncus solitarius aorticus (pulmonary atresia). The first case described was in an infant 6 months of age in whom there was a history of increasing cyanosis and dyspnea. The roentgenograms were atypical and showed an enlargement upward and to the right. There was a rough systolic murmur at the base. The second case occurred in a 3 months old infant with the history of cyanosis since birth and also clubbing of the fingers. No murmurs were heard. Complete autopsy reports are given, together with a comprehensive discussion and bibliography.

BACHMANN, Chicago.

CONGENITAL ATRESIA OF THE HEPATIC DUCTS: REPORT OF CASE WITH OPERATIVE FINDINGS AND AUTOPSY REPORT. S. J. MCCLENDON and H. K. GRAHAM, Arch. Pediat. **48**:791 (Dec.) 1931.

A case of congenital atresia of the hepatic ducts is reported together with operative and autopsy findings.

WADDELL, JR., University, Va.

DIAPHRAGMATIC HERNIA ACCOMPANIED BY DEXTROCARDIA: REPORT OF CASE. ALFRED V. SALOMON, Arch. Pediat. **48**:802 (Dec.) 1931.

The author reports a case of diaphragmatic hernia associated with dextrocardia. The anatomic findings consisted of dextrocardia, rudimentary development of the lungs, atelectasis and a developmental defect of the left leaf of the diaphragm with herniation of the small intestines, stomach, spleen and part of the liver into the left side of the chest cavity.

WADDELL, JR., University, Va.

THREE CASES OF DUODENAL OBSTRUCTION IN THE NEW-BORN. C. P. LAPAGE, ANNIE E. SOMERFORD and FANNY HOWE, Arch. Dis. Childhood **6**:307 (Oct.) 1931.

Three cases are reported of duodenal obstruction due to a constricting band arising from the superior mesenteric artery. Abnormal mobility of the duodenum seems to be a factor in the cause of obstruction.

KELLY, Milwaukee.

ARACHNODACTYLY ASSOCIATED WITH MUSCULAR HYPOTONIA. W. WILSON INGRAM, M. J. Australia **2**:238 (Aug. 22) 1931.

The author reports a case of arachnodactyly or spider fingers in a child aged 2½ years. In addition to the long and slender digits of the hands and feet the

patient showed excessive width between the orbital fossae, absence of the lobules of the ears, a high arched palate, a small mouth, congenital disease of the heart, mental retardation and generalized muscular hypotonia.

GONCE, Madison, Wis.

FIVE CASES OF INHERITED CHONDRODYSTROPHY IN ONE FAMILY. LILLY FRANK, Kinderärztl. Praxis **2**:160 (April) 1931.

Five cases of severe chondrodystrophic dwarfism, in a father and four children, are reported from Budapest. The mother was well and normal in size. A carefully obtained family history failed to reveal any other cases among forbears or relatives.

HUENEKENS, Minneapolis.

COMBINED MALFORMATION OF THE BRANCHIOGENIC ORGANS AND CONGENITAL ABSENCE OF THE PARATHYROID GLANDS. R. RÖSSLE, Virchows Arch. f. path. Anat. **283**:41, 1932.

Only a few thorough examinations of the upper mediastinal and cervical region of the infant have been made with serial sections. In this part of the body three important glands are formed: the thyroid, parathyroid and thymus. Very little is known about the pathologic conditions connected with hypoplasia or absence of these organs during early life. Malformations of the branchiogenic organs as persistent or aberrant ducts are not infrequent. The author has observed several cases in which aberrant thymus tissue was found near the parathyroid or at the site of a thyroid lobe. The present paper deals with two cases in which the organs of the neck were taken out *in toto* and serial histologic sections were made. The first case was that of an acranial, anencephalic child who lived for only nine hours and who had several other malformations. Macroscopically, thyroid tissue was present only on the left side; no evidence of it could be found on the right. A thymus with two large lobes was seen. On the right an accessory lobe of thymus was found at the place where the lower pole of the right missing thyroid lobe should have been. This lobe was not connected with the rest of the thymus gland. All through the thymic tissue, numerous small hemorrhages were noticed. Histologic serial sections showed a small branchiogenic cyst. No evidence of parathyroid tissue could be detected. On the left side between the lobe of the thyroid and the trachea, aberrant thymus tissue was found, the branches of which communicated with the thyroid tissue.

The second case was that of a 10 weeks old girl who suffered from convulsions from the sixth week of life. During the last eight days attacks of choking were observed. The Chvostek sign and peroneal reflex were positive. The clinical diagnosis was tetany. At autopsy, multiple anomalies were found, among which the marked hypoplasia of the pectoral part of the thymus, lack of the isthmus of the thyroid and accessory spleen and pancreas were the most important ones. Besides this, an old hemorrhage in the inside of the dura and corresponding congestion of a part of the arachnoid and pia were found. Again serial sections were made, but owing to a misunderstanding only every tenth section was examined. On the left side a cordlike cervical thymus was present which reached up to the submaxillary gland. Further down, in connection with the left lobe of the thyroid, another thymus "anlage" was found. The thyroid was of slight glandular structure and free from colloid. At the usual site of the thymus, two tiny lobules of thymic tissue were seen. No evidence of parathyroid tissue was detected, but at the right a questionable formation at the posterior median edge of the right thyroid lobe was seen. There is only one other case of this kind in the literature, according to Rössle, that of Böttiger and Wernstedt. They observed a 4 months old girl who died during an attack of laryngospasm due to tetany. In this case a thymus was not visible at autopsy; at its site some fat tissue was found; the thyroid weighed 1.57 Gm. At the right side of the neck, four tiny lobules of thymic tissue were detected which showed normal structure. One very small parathyroid gland was found surrounded by thyroid tissue in the lower posterior part of the right thyroid.

The author discusses the relation between the fatal tetany in these two cases and the lack of parathyroid and thymic tissues. He agrees with Böttiger and Wernstedt that the lack of thymic tissue probably does not play a rôle in the pathogenesis of tetany. The evidence for the secretory activity of the thymus is not sufficient at present to draw any conclusions concerning the function of this organ. Rössle stresses the fact that infantile as well as adult tetany can be due to an insufficiency or absence of the parathyroid glands. These cases are of interest because they throw some light on some cases of infantile tetany during the first months of life for which an adequate explanation has not been given.

SCHOENTHAL, New York.

EVENTRATION IN A HUMAN TWIN. VLADIMIR TUMA, Časop. lék. česk. **69**:324 (Feb. 21) 1930.

The author presents photographs and descriptions of a twin with separation of the spine and an eventration of the liver, spleen, stomach and large and small bowel, and cystic spina bifida. The embryology is discussed. STULIK, Chicago.

STILLBIRTH IN A CASE OF "AX-CUT" DEFORMITY OF THE UTERUS. E. M. STEENBERG, Acta obst. et gynec. Scandinav. **11**:359, 1931.

The author reports a case of intrapartum fetal death due to partial tetanus uteri, producing a so-called "ax-cut" deformity of the uterus. The case reported is that of a primipara in whom labor progressed slowly, in spite of strong pains. The dead fetus showed signs of having been exposed to intra-uterine circular compression, which not only disturbed the relation between the uterus and placenta but also gave rise to ischemia of the lower portion of the fetal body and hyperemia of the head and upper portion. The diagnosis at autopsy was strangulation of the thorax, intra-abdominal hemorrhage, subscapular hematoma of the liver, ecchymoses of the pleura, pericardium and thymus, complete atelectasis of the lungs in prematurity and congestion of the pia mater. The author suggests that the palpated "ax-cut" deformity corresponded to a partial tetanic condition of contraction in the uterine wall, and that this contraction delayed the progress of labor and produced the abnormal condition in the fetus. ADAIR, Chicago.

A CASE OF DYSOSTOSIS CRANIOFACIALIS. L. B. DE MONCHY, Maandschr. v. kindergeneesk. **1**:144 (Dec.) 1931.

A typical case of craniofacial dysostosis in a premature infant is described. The fact that ossification of the coronal suture existed at birth is regarded to be especially in favor of the supposition that the deviation is caused by a factor acting early in fetal life. VAN CREVELD, Amsterdam, Holland.

Diseases of the New-Born

THE RELATIONSHIP OF DERMATITIS EXFOLIATIVA NEONATORUM RITTER AND IMPETIGO BULLOSA IN THE ADULT. SAMUEL J. ZAKON, Arch. Dermat. & Syph. **24**:830 (Nov.) 1931.

The author states that the etiology of dermatitis exfoliativa neonatorum Ritter is as yet not definitely established. Many opinions were expressed in the literature. Zakon reports two cases that meet the clinical postulates of Ritter. In case 1, a normal healthy infant had the lobes of the ears perforated on the third day with resultant impetiginization of the wounds. Within forty-eight hours, an erythema and vesicles appeared on face and neck and then spread rapidly over the body, so that by the sixth day exfoliation took place over most of the body surface. The infant died on the eighth day. In case 2, large bullae and blisters developed on the thighs of the mother of the child. She recovered. The father and one aunt who

had contact with the infant also had lesions typical of impetigo bullosa. The author believes that the two conditions are the same, and that the difference in the biology of the skin of the infant and of the adult led to the difference in clinical appearance.

HENNING, Iowa City.

THE POSTURAL TREATMENT FOR CEREBRAL HEMORRHAGE IN THE NEW-BORN. EDWIN A. RIESENFELD, Arch. Pediat. **48**:728 (Nov.) 1931.

The author comments on the wide variation in the figures representing the incidence of intracranial hemorrhage in the newly born. Predisposing factors, symptomatology and the usual methods of treatment are reviewed. A postural procedure is suggested as a prophylactic measure for, and treatment of, intracranial hemorrhage in the newly born. Riesenfeld advocates placing the infant in an almost vertical position with the head slightly extended and maintained in this position by small pillows placed along the sides of the infant, snugly fitting the space between him and the side of the crib. This position is more easily controlled by placing a blanket completely around the body, enclosing the arms and extending to the neck. The beneficial effects of postural treatment consist of a gradual lessening of symptoms. Clinical and limited experimental data supporting this postural method of therapy are presented. A lessening in pressure readings on the cerebrospinal fluid of patients in the upright position would tend to establish the rationale for this method of therapy. In the upright position, the sagittal venous pressure is materially lessened as determined by experiments on animals, and the author feels that this would seem to be a logical position in treating patients for bleeding from a torn cranial vein.

WADDELL, University, Va.

IMPETIGO CONTAGIOSA NEONATORUM. IRWIN RUBELL, Arch. Pediat. **48**:777 (Dec.) 1931.

A report of a severe epidemic of impetigo contagiosa neonatorum is presented. The literature on this subject is reviewed. Three cases, congenital in origin, are reported in detail. The infecting organism was found to be a staphylococcus. The best procedure for controlling the epidemic consisted of special sterilizing and handling of linen and a series of nurseries for well and infected infants. Special nurses were provided for each nursery, and all attendants were required to conform to a special technic consisting of the wearing of cap, gown and sterile gloves and the liberal use of soap and water for the hands. Of all the procedures inaugurated, proper sterilization and handling of linen and the prevention of overcrowding seemed of chief importance.

WADDELL, JR., University, Va.

DEHYDRATION FEVER OF THE NEW-BORN. F. H. CLARK, Arch. Pediat. **48**:798 (Dec.) 1931.

The author reviews some of the literature on dehydration fever of the newborn, and discusses the symptomatology and treatment. Sixty cases are analyzed from the standpoint of temperature, seasonal occurrence, weight, sex, number of pregnancies, type of delivery and most frequent symptoms and signs.

WADDELL, JR., University, Va.

TWO OBSERVATIONS OF ROENTGENOTHERAPY IN THE COURSE OF GESTATION WITH DELIVERY OF HEALTHY INFANTS AT TERM. LACOMME, Bull. Soc. d'obst. et de gynéc. **20**:457 (June) 1931.

Because exposure of the fetus to the action of x-rays is supposed to be harmful, Lacomme publishes the reports of two cases in which no injury to the child resulted when the mother was exposed to roentgenotherapy during pregnancy. When four months pregnant, a woman, a quadripara, aged 39, because of a diagnosis of fibroma was given roentgen treatments, one each day for five consecutive

days. Each treatment lasted one and one-half hours. The child was delivered at term, was normal in every way and was well and healthy at the age of 3 years, when last seen. The mother had two normal pregnancies after this child was born. The second woman, also a quadripara, aged 37, was given roentgenotherapy for a fibroma. During the second and third months of pregnancy she received thirteen treatments of 400 R. each. The child was delivered at term and was normal in every way. During the second year rickets developed, which the author attributes to poor regulation of feedings.

TURNER, Chicago.

ICTERUS OF THE NEW-BORN. P. LEREBOULLET, J. GOURNAY and J. DETROIS, Nourrisson **19**:356 (Nov.) 1931.

Physiologic icterus of the new-born appears from the second to the fourth day, attains its maximum intensity by the seventh day and disappears entirely by the twelfth day. In the present study, the blood serum and urine of eighteen infants was studied. The degree of cholemia was determined by the Fouchet and van den Bergh reactions. The indirect reaction was always obtained with the latter and averaged 9 units. The erythrocyte counts showed a polycythemia. Red cell fragility tests showed a normal or an increased resistance to saline solution in the majority of the cells studied. Urinalyses for urobilin and urobilinogen gave negative results in five cases and showed only traces in six other cases.

Based on these observations, the explanation is offered that before birth the excess of bile pigment in the serum is removed through the placental circulation. After birth this escape is shut off, and the liver is still functioning too inadequately to secrete the pigment in the normal bile excretion which occurs later. The destruction of the excessive number of red cells present at birth is believed to be a contributing factor. The absence of choluria is thought to be due to the inability of the kidneys to excrete bile during the first few days of life. As soon as the liver and kidneys take on their regular functions, the icterus disappears.

McCLELLAND, Cleveland.

URIC ACID INFARCTS IN THE STILLBORN INFANT. M. BOGEN, Deutsche Ztschr. f. d. ges. gerichtl. Med. **17**:426, 1931.

Ever since the first observations of Virchow (1847), it has been thought that uric acid infarcts are found only in new-born infants who have breathed, and consequently a certain medicolegal significance has been attached to such infarcts. But as far back as 1900, the Hektoen and Riesman textbook emphasized that such infarcts occur also in stillborn infants. The appearance of uric acid infarcts in kidneys of infants who die shortly after delivery seems to have a certain relation to uric acid formation due to the disintegration of large numbers of leukocytes, since in the first days of extra-uterine life there is pronounced leukocytosis. The author describes a pertinent case of a full term but stillborn child, whose dead body was delivered by means of cephalotripsy. Because of the protracted delivery in this case, it is assumed that, as demonstrated in such instances by Schwarz and Mausloff, the umbilical blood contained a large amount of uric acid, which, in connection with disintegration of large numbers of leukocytes, might cause the infarcts, regardless of whether the child was born alive or dead.

MILOSLAVICH, Milwaukee [ARCH. PATH.].

BIRTH INJURIES IN THE NEW BORN: VII. BIRTH INJURIES IN CASES OF ECLAMPTIC LABOR. HIDEO YAGI, Jap. J. Obst. & Gynec. **14**:183 (June) 1931.

The mortality of fetuses and infants born to eclamptic mothers is high (about 50 per cent). Intracranial injuries were found in 57 per cent of cases at autopsy. The hemorrhage was generally marked. These frequent injuries are explained by the prevalence of the causative factors of resistance, pressure and stasis in these eclamptic cases. There is a close relationship between so-called neonatal

eclampsia and intracranial hemorrhage. Other newly born infants with intracranial bleeding present the same symptoms as those with eclampsia neonatorum.

ADAIR, Chicago.

BIRTH INJURIES IN THE NEW BORN: VIII. RELATION BETWEEN ASPHYXIA NEONATORUM AND INTRACRANIAL HEMORRHAGE; TREATMENT AND PROPHYLAXIS OF BIRTH TRAUMATA. HIDEO YAGI, Jap. J. Obst. & Gynec. **14**:191 (June) 1931.

The author proposes that two types of asphyxia neonatorum be recognized on the basis of findings at autopsy: (1) asphyxia suffocatoria and (2) asphyxia apoplectica. There is no good method of differentiating them clinically. The author recommends the following methods of treatment: 1. Aspiration of amniotic fluid and mucus by means of the tracheal catheter, with massage and a warm bath. 2. In more severe cases, a hot bath with gentle methods of artificial respiration; cardiac and respiratory stimulants. The treatment for intracranial hemorrhage is prophylactic and palliative. Sedatives should be used as indicated; the temperature should be regulated; oxygen and stimulants may be used as needed. Lumbar puncture may give results of value. The three main causative factors are resistance of the infant, pressure and stasis. One should aim to prevent premature birth. Nephropathy and syphilis are frequent causes of premature births, so these should be properly treated. The proper management of labor is the best means of preventing intracranial injury, i. e., prophylactic obstetrics.

ADAIR, Chicago.

RELATION BETWEEN MENSTRUAL PERIODICITY AND DURATION OF PREGNANCY. III. MENSTRUAL PERIODICITY AND DEVELOPMENT OF THE NEW-BORN. J. NAKAGAWA, Jap. J. Obst. & Gynec. **14**:400 (Oct.) 1931.

The author has studied the relationship between the duration of the menstrual cycle, the size of the newly born infant and the duration of pregnancy. He excluded all cases in which the infant weighed less than 2,000 Gm. and was not 40 cm. in length. There were 1,348 patients with a regular menstrual cycle to whom infants were born with an average length of 51.47 ± 0.06 cm. and a weight of 3,032.22 ± 7.69 Gm. In a smaller group of 283 patients with an irregular menstrual cycle, the corresponding figures were 50.87 ± 0.13 cm. and 2,998.26 ± 17.41 Gm. The combined series gave figures as follows: 51.36 ± 0.05 cm. and 3,026.33 ± 7.04 Gm. A comparison between male and female infants showed the former to be 0.5 cm. longer and about 100 Gm. heavier. Nakagawa also compared the types of menstrual cycle with the length and weight of the infants, but found no significant variation. The author concludes that there is no relationship between the type of menstrual cycle and the length and weight of the newly born or between this cycle and the duration of pregnancy.

ADAIR, Chicago.

Acute Infections

MEASLES WITH HEMORRHAGIC MANIFESTATIONS: REPORT OF CASE. ISRAEL BINDER, Arch. Pediat. **48**:795 (Dec.) 1931.

The author reports a case of measles complicated by hemorrhagic nephritis, otitis media, lobar pneumonia and mastoiditis.

WADDELL, JR., University, Va.

AN ELECTROPHORETIC STUDY OF THE STERILE FILTRATES OF CULTURES OF THE STREPTOCOCCI OF SCARLET FEVER AND ERYSIPELAS. LAWRENCE E. SHINN, J. Infect. Dis. **49**:281 (Oct.) 1931.

One must read this article in the original to appreciate the data and curves presented. The experimenter concludes that the organisms of scarlet fever and

erysipelas "produce similar but distinctly different changes in the electronitrogen picture. . . . The buffer action changes in growth are different." The toxin of scarlet fever alters its charge between p_H 7.03 and p_H 7.38, and as such does not exist as a simple free substance in the filtrate. In a most interesting introduction the author admits what clinicians have long held, that microscopic cultural or purely chemical methods will not serve to differentiate these types of streptococci.

TOOMEY, Cleveland.

THE VARIOUS COLONIES OF HEMOLYTIC STREPTOCOCCI IN SCARLET FEVER. RUTH TUNNICLIFF, J. Infect. Dis. **49**:357 (Oct.) 1931.

The atypical hemolytic streptococci isolated alone or in conjunction with typical Streptococcus scarlatinae from patients during convalescence from scarlet fever are dissociants from the original typical S. scarlatinae, since in cultures they revert both immunologically and in colony formation to typical S. scarlatinae.

TOOMEY, Cleveland.

STUDY OF THE PREVALENCE OF EPIDEMIC MENINGITIS 1915-1930. A. W. HEDRICH, Pub. Health Rep. **46**:2709 (Nov. 13) 1931.

The author gives a résumé of the history of epidemics of meningitis and a regional study of the last fifteen years. He concludes that during epidemics a large proportion of the population may become infected. During such epidemics half of the patients in the reported cases may die. The interval between the last two epidemics was eleven years in the United States. In 1918 the southern section had the highest attack rates and the Rocky Mountain states the lowest. In 1928 this was exactly reversed.

SANFORD, Chicago.

SCARLET-FEVER STREPTOCOCCUS ANTITOXIN IN THE TREATMENT OF SCARLET FEVER. M. V. VELDEE, F. E. STEVENSON and A. G. MITCHELL, Pub. Health Rep. **46**:3023 (Dec. 18) 1931.

The authors studied the results shown in 112 patients with scarlet fever given antitoxin as compared with the results in 84 not given it. The study showed that the antitoxin has a specific neutralizing effect on the toxin, as indicated by a decrease in the duration of the rash, a change in the extent of the desquamation and a reduction of complications. That it fails to neutralize completely is shown by the failure of the rash to disappear promptly, by the continuation of the fever and by the appearance of complications in a certain number of patients treated with serum. This may have been due to (*a*) too small a dose, (*b*) an improper method of administration, (*c*) administration too late in disease or (*d*) the inadequacy of the antitoxin to neutralize all the toxic substance elaborated in this disease. The early administration of antitoxin and its rapid dissemination are essential. The probability of serum-sickness must be weighed. The frequency of this complication cannot be attributed entirely to the serum itself; previous sensitization to horse serum plays an important rôle. With the introduction of toxoid instead of toxin-antitoxin, there will be a corresponding reduction of this complication. It is also hoped that the volume of the therapeutic dose may be reduced.

SANFORD, Chicago.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **46**:3115 (Dec. 25) 1931.

For the period from Nov. 8 to Dec. 5, 1931, poliomyelitis showed a marked decrease, as did scarlet fever, smallpox, meningitis, typhoid fever and influenza. The rates for diphtheria and measles were higher. The mortality from all causes was the lowest in six years, 11.1 per thousand.

SANFORD, Chicago.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. For the period of Dec. 6, 1931, to Jan. 2, 1932. Pub. Health Rep. **47**:185 (Jan. 22) 1932.

Measles, scarlet fever and diphtheria showed the usual seasonal increase, with the incidence of diphtheria 22 per cent, and of scarlet fever 10 per cent, in excess of that for the previous year. Poliomyelitis had declined 60 per cent. The mortality rate was 11.4 per cent, the lowest in six years for the corresponding period.

SANFORD, Chicago.

PURPURA AS A COMPLICATION OF SCARLET FEVER. F. G. WOOD-SMITH, Brit. J. Child. Dis. **28**:273 (Oct.-Dec.) 1931.

Purpura as a complication of scarlet fever is rare and is most frequently met with in children. "That purpura is probably due to bacterial action is indicated by its connection with well known bacterial disease, and by the fact that in some cases an organism has been isolated from the blood." There is no doubt that the capillary walls become damaged. The thrombopenia that is often met with in this condition is difficult to explain, mainly on account of its inconsistency. The purpuric spots or ecchymoses usually appear during the third week of the infection. In mild cases the lower limbs only are affected. The death rate is high, and in the fulminant type death may occur in forty-eight hours or sooner. The author describes a case in a man aged 26 years who was treated with antistreptococcal (scarlatinal) serum on the sixth day of the disease and in whom purpuric spots developed on the upper and lower limbs on the fifteenth day. Several crops of purpuric spots appeared, the last on the forty-fifth day. After that day a normal convalescence ensued.

LANGMANN, New York.

AN AGGLUTINATION CURVE IN TICK-BITE FEVER. ADRIANUS PIJER and HELEN DAU, J. M. A. South Africa **5**:519 (Aug. 22) 1931.

One of the authors permitted herself to be bitten by larval ticks in an infected neighborhood. She developed typical tick-bite fever (not tick-fever or relapsing fever), which ran a typical course of bite mark, regional glandular swellings, papular rash, high fever and severe headache. Symptoms appeared on the eleventh day after exposure, and the acute symptoms lasted nine days. Specimens of serum taken from the patient before, during and after the acute manifestations of the disease were tested for agglutination reactions against Bacillus proteus O X 19, B. proteus O X 2 and B. proteus X, Kingsbury. The agglutination titer on the day after the bite was 1:20 against all three strains, and at the time of the onset of acute symptoms was 1:100 against X 2 and X 19, and 1:200 against X Kingsbury. Then, the titer against X 2 and X 19 fell off to 1:40-50, rising again in late convalescence to 1:100, and against X Kingsbury steadily increased up to a maximum of 1:425 for a short time in early convalescence and to 1:325 in late convalescence. In other patients in whom tests were made late in the disease or in convalescence equal titers for all three B. proteus X strains were found. This work indicates that specific agglutinins against tick-bite fever exist, and that their titer is increased during disease and convalescence.

GONCE, Madison, Wis.

A NEW MEDIUM FOR DIFFERENTIATING FORMS OF DIPHTHERIA BACILLUS. J. ANDERSON, F. HAPPOLD, J. MCLEOD and J. THOMSON, J. Path. & Bact. **34**:667, 1931.

There are two principal forms of the diphtheria bacillus. B. diphtheriae-gravis is associated with severe toxic cases of the disease. It grows with granular deposit and pellicle in broth, has a flattened lusterless colony of irregular outline and actively ferments polysaccharides. B. diphtheriae-mitis is associated with milder

cases of disease in which there may be extensive membrane formation without serious intoxication, and which is probably chiefly dangerous from laryngeal involvement and obstruction of breathing. This form grows with uniform turbidity on broth, has a convex, partly translucent and light-reflecting colony and does not ferment polysaccharides. In addition, there have been observed from 5 to 10 per cent of intermediate forms giving granular growth in broth but failing to ferment starch, etc. The strain Park Williams 8 falls into this class. So far as they have been observed, the characters of these different forms are fixed. A blood agar medium is described, prepared with slightly heated broth sterilized by infiltration, and containing 0.04 per cent potassium tellurite, which permits determination of the presence or absence of B. diphtheriae at sight in 90 per cent of cultures from throat swabs after from eighteen to twenty-four hours of incubation. It also gives with the gravest types of diphtheria, those associated with B. diphtheriae-gravis, a picture so characteristic that it is not likely to be confused with anything else.

AUTHORS' SUMMARY [ARCH. PATH.].

INFECTIOUS DISEASES IN PUBLIC SCHOOLS: THEIR ORIGIN, SPREAD AND PREVENTION. L. R. LEMPRIERE, Practitioner **128**:1 (Jan.) 1932.

The author presents an excellent article dealing with the problem of infectious disease in the public school of England. In 1885, "A Code of Rules for the Prevention of Infectious Diseases in Schools" was published in an endeavor to make a uniform plan to be carried out in all public schools. The "Code" has been modified a number of times, but still remains the school doctor's guide and authority. In a review of six large public schools in which careful records have been kept, Lempriere has tabulated the following epidemic diseases: measles, rubella, varicella, mumps, scarlet fever and pertussis. An analysis of these shows that, although the rules laid down by the "Code" have been faithfully followed from twenty to forty-five years, the system has been a failure with respect to diminishing the total number of cases and the incidence of these infections. Comparisons were made on the basis of a ten year period in order to rule out the results of an exceptional single year. The author feels that the main sources of origin of epidemics are the infections brought into the schools during the first three or four weeks of a new term. Also, a number of epidemics arise during the term owing to home visits, visits of the family at school or other contact with professors' families, servants, tradespeople and others. With respect to the spread of infection, the author stresses the importance of overcrowding in the schools. The extent of an epidemic is governed largely by the nature of the infective agent, whether there are one or more foci, and the "herd immunity." Measles is the only infection however, that is at all constant, but with this disease one may expect four fifths of all susceptible persons to be attacked during an epidemic. The duration of an epidemic is, likewise, extremely variable.

As to immunity, Lempriere, from his study of the records showing immunity on entrance into school, feels that boys of today are perhaps better protected than were their fathers of twenty or thirty years ago. An interesting point disclosed by the study is that sporadic cases made up from 28 to 34 per cent of the total number of cases in any given period at the various schools. A discussion of preventive measures is given, including the use of the Dick and Schick tests for diagnostic purposes and the use of measles convalescent serum. Although the results of the prolonged trial of public health measures for the prevention of the introduction and spread of disease have been a failure from the narrow point of view, the author points out that the community at large definitely benefits, as illness increases "herd" immunity, and also that persons are affected at a period when loss of time is relatively less costly to them.

SAPPINGTON, San Francisco.

PRACTICAL ASPECTS OF MEASLES. WILLIAM GUNN, Practitioner **128**:19 (Jan.) 1932.

In this interesting article, the author discusses the problem of measles with reference to the condition in London. He states that measles causes more deaths than all other common infections combined, and that age is the most important single factor determining both the incidence and the prognosis of the disease. The biennial recurrence of measles results from the accumulation of a susceptible population between epidemics. The highest rate of attack occurs in the 3 to 4 year group. The fatality rate is greatest during the first year, but remains high until the third year, when it falls rapidly until after five years the disease appears to be rarely fatal; hence the value of measures that will defer attacks to later age groups. Gunn believes that after the age of 3 years, absolute protection is not needed, but it is desirable to employ one of the modern methods of modifying the severity of attack and by this method secure a permanent immunity. He states that should a child still escape attack after 5 years of age, it would be wise to expose him deliberately and insure attenuation by the use of serum. In this manner the entire population would be rendered immune under most favorable conditions. This plan requires the availability of convalescent serum supplied by the local health departments. To afford complete protection a minimum dose of 5 cc. is injected intramuscularly during the first five days after exposure, and from the age of 3 years upward the dosage in cubic centimeters of serum is determined by multiplying the age in years by two. To provide just enough serum for an attenuated attack, the same dose is injected between the sixth and ninth days after exposure. Equally favorable results may also be obtained by the intramuscular injection of adult whole blood from a parent who has previously had measles. The dose, both for prevention and attenuation, is double that of convalescent whole blood and four times that of convalescent serum. When sero-attenuation is practiced, the attack following exposure is always mild and uncomplicated. The resultant immunity is usually complete and permanent.

SAPPINGTON, San Francisco.

SOME ASPECTS OF MUMPS. J. D. ROLLESTON, Practitioner **128**:31 (Jan.) 1932.

In this excellent article, including a good review of the literature, Rolleston discusses mumps under the headings of bacteriology, pathology, clinical aspects, complications, diagnosis, prognosis, prophylaxis and treatment. According to Kermorgant, mumps is due to a spirochete present in the saliva at the onset of the disease. Capitan, in the observation of 700 cases, found enlargement of the spleen in almost every case. One attack confers permanent immunity, and second attacks are so rare that many men of wide experience have not seen any. Orchitis is by far the most common complication. Capitan, in his 700 cases in soldiers, found it varied from 15 to 25 per cent, depending on the period of years considered. Pancreatitis, encephalitis and meningitis are interesting complications also discussed. The use of convalescent serum has not been found to be satisfactory so far. The author states that there are no specific recommendations as to treatment, although in view of the supposed spirochetal origin, injections of arsphenamine have been suggested.

SAPPINGTON, San Francisco.

THE CONTROL OF SCARLET FEVER. NORMAN HALLOWS, Practitioner **128**:40 (Jan.) 1932.

In scarlet fever three problems of importance must be considered, i. e., diagnosis, specific treatment and prevention. Early accurate diagnosis is not always easy, but the author feels that the physician should be conservative. As to etiology, Hallows states that recent investigators have typed certain streptococci which are responsible for scarlet fever and allied infections. According to Griffith, there are four main types and also a heterogenous group. Types I, II, III and IV were found in approximately two thirds of the cases. As to complications, it

was noted that type I more frequently gives rise to otitis media and type II to diphtheria. The author points out the value of the Dick test in determining susceptible persons and the value of the Schultz-Charlton reaction as an aid to diagnosis. Hallows believes in the value of immunization and active treatment, and states that the results of serotherapy are most encouraging. His regulations with respect to the duration of quarantine are: "If a patient be free from discharges, sore or enlarged glands, he may be discharged with safety at the end of four weeks, irrespective of desquamation." SAPPINGTON, San Francisco.

DIPHTHERIA. W. T. BENSON, Practitioner **128**:47 (Jan.) 1932.

A brief résumé is given of the early history of diphtheria with a clearcut description of the etiology, pathology and symptoms. Under complications, the author points out that the incidence of diphtheritic paralysis varies from 10 to 20 per cent, depending on the severity of the attack. He emphasizes that cardiac failure may occur within a few days of the onset of illness or any time up to the second or third week following. He mentions that interference with the function of the soft palate is the commonest early manifestation of diphtheritic paralysis. The differential diagnosis covers the conditions of Vincent's angina, follicular tonsillitis, measles and scarlet fever. Benson stresses the point that the recognition of diphtheria rests primarily with the clinician, and that too much weight must not be given to negative results of bacteriologic examination. The prognosis of any case depends largely on the early diagnosis and efficient treatment with antitoxin. Under treatment, the author states: "Clinical experience indicates that a range of antitoxin dosage from 2,000 units in the mildest cases to 50,000 units in the hypertoxic patient may be regarded as sound practice. Some authorities advocate relatively enormous doses, up to 300,000 units in malignant attacks. In gross toxemia or laryngeal involvement 10,000 to 30,000 units should be administered intravenously. A large primary dose is preferable to smaller injections spread over two or more days. As a general rule the intramuscular route should be adopted. The lateral aspect of the thigh is an excellent site for injection. Rest for ten days in the recumbent position, recommended for the mildest case, should be extended to a minimum of six weeks in a severe attack. Trained nursing, always advisable, is essential in all except the mildest cases. The author makes it clear that the treatment of laryngeal diphtheria is a matter for the specialist who is expert in aspiration, intubation or tracheotomy. The question of carriers and their treatment is given due consideration. The subject of prevention is discussed and the author's method of immunization outlined.

SAPPINGTON, San Francisco.

THE TREATMENT OF WHOOPING COUGH. ARTHUR J. TURNER, Practitioner **128**:66 (Jan.) 1932.

After a discussion of the various methods that have been tried, the author presents his plan for the treatment of pertussis. He says that the use of the Bordet-Gengou vaccine has not been successful enough to warrant its general use, and he also states that the same may be said for the use of intramuscular injections of ether. Turner quotes E. H. and W. K. Russell who reported the use of ultraviolet irradiation in a large number of cases with uniformly successful results. The details of the author's method of treatment are: "The entire body is exposed to the ultra-violet rays at a distance of 36 in., the patient lying down, first on the back and then prone. Until the principal symptoms had disappeared this exposure was made once a day and then twice a week for one or two weeks. The first dose varied with the age of the child from half a minute to two minutes both to back and front. Each day the dose was increased, in the youngest by half a minute each day, in older ones by one minute each day. I am not a believer in large doses, especially when given every day, as it is very important not to produce any pigmentation of the skin, such pigmentation when produced tending

to obstruct the passage of the rays." Turner used this method in his cases of pertussis over a three year period and states that his success has been almost identical with that of the Russells. The symptoms disappeared and the patients were apparently cured on the average in twenty days.

SAPPINGTON, San Francisco.

MEASLES AND CUTANEOUS REACTION FOR TUBERCULOSIS. P. LEREBOULLET and P. BAIZE, Arch. de méd. d. enf. **34**:701 (Dec.) 1931.

Pirquet and Preisich, in 1907, demonstrated that children suffering from measles lost temporarily the power to react to tuberculin. The cutireaction disappears at the onset of this infection, remains negative for about one week and then reappears. Mantoux and Harvier have since shown similar phenomena attending the intradermal method. Interpretation of this peculiarity is not easy. Pirquet suggested the following explanation: In subjects previously infected with tuberculosis, the organism is modified for the entire life, and possesses the power to form ergins and antibodies much more rapidly than before the invasion. This property is termed allergy, and the positive reaction of the skin to tuberculin may be considered as a witness of the allergic state. When tuberculous children contract measles, the absence of the skin reaction may be construed as an absorption or mobilization of the ergins, which temporarily brings about a diminution or complete suppression of allergy and establishes a state of anergy or heightened receptivity to tuberculous infection. For this reason, measles has long been considered favorable to the dissemination of phthisis. Recent authors, however, especially Debré and his pupils, declare that this view is not borne out in the clinic. They scout the idea of a phthisiogenetic rôle in measles, and seek to explain the disappearance of the tuberculin reaction by considering it as a purely cutaneous response in the presence of the morbilliform exanthem. However one regards it, authorities agree that if measles does not actually produce a tuberculous state, it aggravates a preexisting infection and may reactivate a latent focus.

The authors had an opportunity throughout the year 1930 to note the relation between the cutireaction and the clinical course of measles, the tuberculin used in these observations being furnished by the Pasteur Institute. Among ninety-eight patients, a positive reaction had existed in sixteen; of these only two failed to lose the reaction during the progress of measles, usually toward the thirteenth day after exposure. In half of these the disappearance was sudden; in the others the reaction faded gradually. The reappearance of the response to tuberculin occurred in from fifteen to sixteen days after the onset of the eruption. Seventy-five of the cases were followed for a year; in only one instance was the old tuberculous lesion aggravated and in but two cases did active tuberculosis follow the measles invasion, one patient dying of caseous bronchopneumonia and the other of tuberculous meningitis.

AMESSE, Denver.

ENCEPHALITIS FOLLOWING MEASLES: REPORT OF A CASE. P. LECHELLE, I. BERTRAND and E. FAUVERT, Arch. de méd. d. enf. **34**:718 (Dec.) 1931.

Complications and sequelae of measles, particularly those involving the central nervous system, have been reported with increasing frequency during the past decade. While meningitis or myelitis is more commonly observed, encephalitis is by no means unusual; the authors report such an instance, with complete anatomic studies. A baby, aged 21 months, with a moderately severe invasion of measles was found to be a diphtheria carrier. She was isolated and given a prophylactic dose of antitoxin. On the ninth day, with convalescence apparently well established, she suffered an attack of dyspnea followed by a convulsion; the temperature rose to 104 F., without further pulmonary symptoms. A few hours later convulsive seizures returned and continued for several hours; the spinal fluid was normal. Paralysis of the right side of the face followed, with right hemiplegia and pro-

nounced ophthalmologic phenomena. Coma ensued, with hyperpyrexia and death in twenty hours. Postmortem observations confirmed the diagnosis of encephalitis.

AMESSE, Denver.

DIPHTHERIA ANTITOXIN. A. B. MARFAN, Nourrisson **19**:351 (Nov.) 1931.

Marfan recalls the preantitoxin days, and sites his long experience in the use of antitoxin. He prefers the unconcentrated antitoxin, and emphasizes the necessity of early diagnosis and early administration. The size of the initial dose and the number of subsequent injections depend on the location and severity of the infection. In malignant angina and cases of diphtheritic croup he uses as much as 90,000 units, 40,000 units being given during the first twelve hours. Smaller amounts are used in the milder cases.

MCCLELLAND, Cleveland.

TOXICITY OF THE URINE AND THE EXANTHEM OF MEASLES. F. STEFFEN, Schweiz. med. Wchnschr. **61**:1103 (Nov. 14) 1931.

The author reports studies on the urinary calcium content in two patients with measles and on the toxicity of the urine for animals. Coincident with the onset of the rash, both the calcium content and the toxicity increased to about double the normal values. As the rash cleared, the calcium content and toxicity of the urine fell to subnormal levels. The conclusion is that the toxicity of urine in patients with measles, and presumably with other exanthematous diseases, is due to its calcium content. The literature is quoted to show that the skin is a reservoir of calcium.

WOLMAN, Chicago.

A CASE OF A GONOCOCCIC PELVIC PERITONITIS IN A FIVE YEAR OLD CHILD: CLINICAL RECOVERY. J. M. MACERA, A. L. DOMENCH and F. L. FERNANDEZ, Arch. argent. de pediat. **2**:258 (May) 1931.

The authors describe a case in a 5 year old girl in whom, shortly after a development of a gonococcic vulvovaginitis, a pelvic peritonitis developed, with all its characteristic symptoms. Recovery followed promptly with the use of cold applications, methenamine and vaccine and the administration of foreign proteins.

SCHLUTZ, Chicago.

SYMPTOMS OF INVOLVEMENT OF THE JOINTS FOLLOWING MEASLES. R. CHARLONE, Arch. de pediat. d. Uruguay **2**:80 (Feb.) 1931.

The author describes three cases of measles in which during convalescence severe pain and limitation of motion appeared, due to marked muscular spasm, in both coxofemoral articulations. The interesting feature about this complication is that there was no inflammatory reaction in those joints as far as could be determined by inspection, palpation and roentgen examination. The course was favorable in two of the cases, all the symptoms subsiding in from five to seven days. In one of the patients there was a complicating tuberculous meningitis. As treatment, the author recommended complete rest and Bier's hyperemia.

SCHLUTZ, Chicago.

AN EPIDEMIC OF DIPHTHERIA IN TACUAREMBO. JUAN BAUTISTA GIL, Arch. de pediat. d. Uruguay **2**:574 (Dec.) 1931.

The epidemic described extended over a period of eighteen months. The origin of the disease was never found. It was observed that if diphtheria developed in immunized persons, it was benign and easily cured with small doses of serum. The mortality of diphtheritic angina was low if treatment was begun early and large doses of serum were given. The high mortality of diphtheritic croup was seen only when treatment was begun very late. The size of the dose of serum was not as important as early administration. The same thing was true of the age

of the patient. The gravity of the symptoms and the time of onset of the disease, rather than the age of the child, should govern the size of the dose of antitoxin to be given. The serum was well borne even by the youngest infant. The most severe symptoms were encountered much oftener in older children of the second and third period of childhood than in the young infant. SCHLUTZ, Chicago.

SEPTIC DIPHTHERIA. F. VON BORMANN, Arch. f. Kinderh. **94**:16 (Oct. 23) 1931.

Septic diphtheria, according to the author, is a distinct clinical entity in which there is a dirty green, necrotic membrane covering the pharynx, a fetid breath and marked involvement of the lymphatic ring, with frequent septic complications. It has little in common with ordinary diphtheria, but resembles more a mixed infection of diphtheria and scarlet fever. The finding of the streptococcus in the throat and the pus from an otitis media, for example, and also in the circulating blood establishes the rôle of the streptococcus in this infection. In treatment the "symbiose serum" of Sachs is of more value in bringing about a return to normal in the tissues of the pharynx and the associated lymph glands than is diphtheria antitoxin alone. An early injection is advisable. The serum was found to have no value in combating scarlet fever. LESLIE, Evanston, Ill.

THE CHEMISTRY AND IMMUNOLOGY OF THE EXTINCTION PHENOMENON IN SCARLET FEVER. JULIUS BERENDES, Jahrb. f. Kinderh. **133**:75 (Sept.) 1931.

A critical review of the literature is presented. Berendes found extinction by calcium present in only 10 per cent of cases. Serum diluted beyond 1:80 was inactive. Heating to from 50 to 56 C. does not alter the activity, whereas heating to 70 C. destroys it. Absorbents (animal carbon, salicylic acid, kaolin and talc) do not check the activity. The active fraction is precipitated with the globulin by ammonium sulphate. Ultraviolet irradiation for from forty to sixty minutes or peptic digestion do not destroy the activity. Placental serum is active.

CLAUSEN, Rochester, N. Y.

THE EPIDEMIOLOGY OF DIPHTHERIA WITH SPECIAL REFERENCE TO THE MALIGNANT FORMS. ADOLF GOTTSTEIN, Kinderärztl. Praxis **2**:193 (May) 1931.

A reconsideration of the epidemiology of diphtheria is demanded for three reasons: the increase in the morbidity and mortality of diphtheria, the increase in the severer type, sometimes called malignant and sometimes toxic forms, and finally the increasing conviction that antitoxin has but a slight effect in these malignant cases. Gottstein quotes from the literature and gives some evidence from his personal experience to show that malignant diphtheria is due to familial predisposition. HUENEKENS, Minneapolis.

THE THEORY AND PRACTICAL RESULTS OF IMMUNIZATION TO SCARLET FEVER. HENRYK BROKMAN, Kinderärztl. Praxis **2**:200 (May) 1931.

The person with a positive Dick reaction is much more susceptible to scarlet fever than the one with negative reaction. The change from a positive to a negative Dick reaction after immunization is usually accompanied by the appearance of scarlet fever antitoxin in the blood. Brokman employed four kinds of vaccine: (1) pure toxin, (2) toxin combined with streptococci, (3) anatoxin (toxin treated with a solution of formaldehyde) and (4) anatoxin combined with streptococci killed by means of formaldehyde. In his early work, a total of 3,500 skin test units of pure toxin was given, but this has since been increased to 16,000 skin test units. This dose is contained in 3 cc. of the vaccine. The combined vaccine contains 200,000,000 streptococci per cubic centimeter. Anatoxin is given undiluted (10,000 skin test units per cubic centimeter), the total dosage varying from 1.5 to 6 cc. The first dose is small (0.5 cc.), and from 2 to 3 doses are

given, sometimes at seven day intervals, but preferably from fourteen to twenty-one days apart. No permanent ill effects were discovered. In infants and young children the pure toxin sometimes caused fever, exanthems and vomiting; anatoxin occasionally produced an elevation of temperature, with local pain and swelling, more often in older children and adults. Of 16,345 vaccinated children, who earlier had had positive Dick reactions, 0.37 per cent contracted scarlet fever within a period of eighteen months after vaccination, as compared with 89,818 unvaccinated control children, with positive Dick tests, of whom 1.9 per cent contracted the disease. These figures, however, are from children who had received a total of 3,500 skin test units. No figures are available from the children receiving larger doses. Of the children immunized by Brokman, 75 per cent continued to have a negative Dick reaction after three years.

HUENEKENS, Minneapolis.

EXPERIENCE WITH MIXED PERTUSSIS VACCINE. FRIEDRICH MIELKE, Kinderärztl. Praxis **2**:206 (May) 1931.

The author used mixed pertussis vaccine in fifteen cases in an infants' hospital. He recommends it highly as a prophylactic and therapeutic agent.

HUENEKENS, Minneapolis.

THE PROPHYLAXIS AND TREATMENT OF PERTUSSIS. MAURO GIOSEFFI, Kinderärztl. Praxis **2**:207 (May) 1931.

Gioseffi reports the results of pertussis vaccine in a hundred children. He gives from four to eight intramuscular injections, in varying doses of from 100,000,000 to 1,000,000,000. He is enthusiastic as to its value in the prophylaxis and treatment of pertussis.

HUENEKENS, Minneapolis.

THE BACTERICIDAL EFFECTS OF CHEMICALS: EFFECT OF CHINA-ALKALOIDS, PHENOLS, ACRIDINE-DYES, ETHEREAL OIL, ETC., ON THE BORDET-GENGOU BACILLUS. F. WILDTGRUBE, Ztschr. f. Kinderh. **52**:55, 1931.

The bactericidal effects of fifty-seven different substances on the Bordet-Gengou bacillus were studied. The acridine dyes were found to be the most effective. Acriflavine hydrochloride killed the bacilli in dilutions of 1:8,000 and acridine in dilutions of 1:16,000. Of the China-alkaloids, Eucupinum and Vicinum dihydrochloride were effective in dilutions of 1:3,200. The phenols were only slightly bactericidal. Of the ethereal oils, oil of anise was mildly effective. Neoarsphenamine killed the organisms in dilutions of 1:800 while chaulmoogra oil was totally ineffective. The bactericidal properties were more pronounced in horse serum bouillon than in whole blood bouillon, the difference being due to the binding of the chemicals by the red cells.

SHELLING, Baltimore.

SCARLET FEVER AND LOEFFLER'S BACILLI. VÝMOLA and KOPÁČ, Časop. lék. česk. **69**:90 (Jan. 10) 1930.

Of 205 patients with scarlet fever 27 had diphtheria organisms on their entrance into the hospital. During their illness of four weeks, 12 others showed gross tonsillar evidence of diphtheria with positive cultures, 6 with both nasal and tonsillar positive cultures and 17 with positive nasal and negative pharyngeal cultures. This made a total of 62 cases, or 30.24 per cent, showing positive diphtheria cultures. Of 143 patients with scarlet fever, 23 had ear complications; but of these, 4 had measles as a complication, 1 had croup with a positive diphtheria culture, 1 had nasal diphtheria and one had tonsillar diphtheria, so that 16 (11.77 per cent) cases were considered as simple scarlet fever. Of the 62 cases complicated by diphtheria, 8 (12.9 per cent) were complicated by disease of the ear.

STULIK, Chicago.

RESULTS OF THE INJECTION OF TOXOID IN DIPHTHERIA. W. GLOWACKA, Pediat. polska **14**:163 (May-June) 1931.

The Schick test was performed on 961 children, from 5 to 15 years of age, 80.7 per cent of whom gave positive reactions. These children came from homes with high standards of living in the city of Warsaw. The majority received three weekly injections of toxoid. The results of immunity, shown in a table, were very encouraging. Of 695 children inoculated, about 9 contracted the disease during the period of study.

KRUPINSKI, Chicago.

INOCULATION OF CHILDREN IN THE PUBLIC SCHOOLS OF LODZ AGAINST SCARLET FEVER. STANISLAUS GUTENTOG, Pediat. polska **14**:175 (May-June) 1931.

The Dick test was performed on 9,175 children; about 50 per cent of the 7 year old group gave positive results. The older the children the smaller the number of positive Dick tests. Jewish children gave 10 per cent fewer positive reactions. The majority of the children received three injections, and after six weeks the Dick test was again performed; 34 per cent of the tests were negative. The reactions were not serious; local reactions were observed in 20 cases; 9 children had sore throats and a rash with a temperature of 101 F.; 35 had scarlet fever in a mild form without complications. The period of immunity was from six weeks to four years.

KRUPINSKI, Chicago.

Chronic Infections

PURPURIC MANIFESTATIONS IN TUBERCULOSIS. JOSEPH GREENGARD, Am. Rev. Tuberc. **24**:452 (Oct.) 1931.

In a child aged 3 years purpura occurred during the course of acute miliary tuberculosis. There were numerous cutaneous hemorrhages and an extensive intermeningeal hemorrhage over the left cerebral hemisphere. There was definite diminution of the formed elements of the blood, particularly thrombocytes, but at autopsy no damage to the bone marrow was found. The tourniquet test was positive. In another child, 11 years of age, a typical cachectic purpura occurred during the course of chronic tuberculosis. The thrombocytes were slightly decreased, and capillary damage was indicated by a positive tourniquet test. While it is possible that in some cases the purpuric manifestations in tuberculosis are of an anaphylactoid type, the author believes that capillary damage is an important cause of the condition.

SMITH, Ogden, Utah.

VARIATIONS IN TUBERCULIN SENSITIVENESS IN TUBERCULOUS PATIENTS. SPENCER SCHWARTZ and FRED H. HEISE, Am. Rev. Tuberc. **24**:479 (Oct.) 1931.

A single intracutaneous tuberculin test reveals only a previous infection with tubercle bacilli. No reliable information regarding the extent or nature of the pulmonary lesion or its activity can be obtained by a single test. Likewise, repeated tests give no conclusive information regarding the lesion.

SMITH, Ogden, Utah.

A STUDY OF TUBERCULOSIS IN ONE JUNIOR HIGH SCHOOL IN HONOLULU. S. E. DOOLITTLE, Am. Rev. Tuberc. **24**:491 (Nov.) 1931.

Of 1,437 students tested (from 11 to 18 years of age) 75.57 per cent gave positive tuberculin reactions with cutaneous and intracutaneous tests with doses of 1 mg. Cutaneous tests alone gave 37 per cent positive reactions, less than one-half as many as in the complete series of intracutaneous tests. Roentgenologic examination of all persons with a positive reaction revealed 13 cases of adult pulmonary tuberculosis, 10 cases of suspected pulmonary tuberculosis and 175

lesions classified as of the childhood type (including pleurisy). In nearly all the cases of this last group the condition was latent or nearly healed. The percentage of tuberculous infection in Honolulu is not notably higher than in larger urban communities on the mainland, in spite of a somewhat higher mortality rate from tuberculosis. It is probable that the percentage of infection in different racial groups having varying death rates from the disease is affected only as the opportunity of intimate contact, largely in the home, is increased.

SMITH, Ogden, Utah.

RACIAL SUSCEPTIBILITY TO TUBERCULOSIS. EMIL BOGEN, Am. Rev. Tuberc. **24**:522 (Nov.) 1931.

Bogen believes that the conclusions drawn from many extensive studies on tuberculosis as it occurs in different racial groups are invalidated by the fact that environmental factors governing the extent of exposure and the living conditions of the various groups have been uncontrolled. These factors have been carefully studied in a series of 4,730 institutional patients. It appears from this study that the greatest discrepancy between death rates from tuberculosis in patients of different nationalities, in this institution at least, arises from the fact that some groups are admitted early in the disease and others late, and bears little relationship to any innate differences in their reaction to the infection after it has reached a certain stage. The fact that patients of the different races who were in the same stage of the disease showed only insignificant differences in their mortality rates, speaks strongly against attaching any weight to the factor of race in evaluating the expectancy of survival of a patient with tuberculosis. It is not implied that there are not great differences in the extent of tuberculosis among different groups in the community, or that the gross mortality rates among these groups do not vary widely. It is maintained, however, that these differences tend to disappear if the subjects are taken in the same stage of the disease and subjected to similar environmental conditions.

SMITH, Ogden, Utah.

TUBERCULOUS INFECTION AMONG SCHOOL CHILDREN IN A RURAL AREA IN NEW YORK STATE. JOHN H. KORNS, Am. Rev. Tuberc. **24**:532 (Nov.) 1931.

Of 1,103 apparently healthy school children between the ages of 5 and 19 years from farms and villages, 112 (10.2 per cent) reacted to a quantitative intracutaneous tuberculin test. The rate of infection in villages was 12.6 per cent as contrasted with 6.6 per cent on the farms. The rate among those who had lived in the county since birth was 7.6 per cent, while among those who had resided outside the county for part of their lives the rate was 21.1 per cent.

SMITH, Ogden, Utah.

THE SPECIFICITY OF AVIAN TUBERCULIN REACTIONS. VERA B. DOLGOPOL, J. Infect. Dis. **49**:216 (Sept.) 1931.

Many tuberculous patients give positive avian as well as positive human tuberculin reactions. The author believes that the avian tuberculin reaction may be discounted, especially if it is less than the reaction observed with the human tuberculin material, since she was unable to produce tuberculosis in fowls by any method of injection of material obtained from patients with positive avian tuberculin tests.

TOOMEY, Cleveland.

MYCOBACTERIUM (SP. ?), RYAN STRAIN, ISOLATED FROM PLEURAL EXUDATE. PAUL W. BEAVEN and S. BAYNE-JONES, J. Infect. Dis. **49**:399 (Nov.) 1931.

The authors isolated an acid-fast organism from the pleural exudate of a child which acted totally unlike human strains of tuberculosis, especially as regards

pathogenicity. They state that the organism described is a representative of a distinct group of acid-fast bacteria with low pathogenicity for man and animals.

TOOMEY, Cleveland.

WHAT CAN BE DETERMINED BY THE TUBERCULIN TEST? F. M. POTTENGER, M. J. & Rec. **124**:365 (Oct. 9) 1931.

A child showing a quick and marked response to a tuberculin test should be considered as having an active infection which is at the time or has in the recent past been giving off sensitizing substances into the circulation. This is evident because the primary complex in the child produces sensitization of the cells which may be maintained or increased until calcification takes place. For any degree of desensitization to take place in the natural course of infection, quiescence or healing of the lesion is necessary. Children who are in normal health and react positively to tuberculin tests need no special care beyond observation with reexaminations and repeated tests made every six months. Those who are below par and who show signs of tuberculosis and a positive tuberculin test should be given attention that will help to secure a complete healing of the foci. When a negative reaction is obtained in these children, the test should be repeated when the health has improved. Roentgenograms should be taken of all children who react to tuberculin, and one should remember that while the primary lesion is in the lung in 85 per cent of children many of the lesions cannot be visualized unless they are partially or wholly calcified, even if they are favorably located. The presence of a fully calcified mode is not so serious as that of a partially or, particularly, a wholly uncalcified one.

WILLIAMSON, New Orleans.

A DISCUSSION OF THE MECHANISM OF IMMUNITY WITH CALMETTE'S VACCINE. B. FRIAS and E. J. ROLDAN, Arch. de méd. d. enf. **34**:713 (Dec.) 1931.

While few deny the vaccinating properties of B C G against tuberculosis, there is not so common an accord in the interpretation of its action. From anatomic studies made by the writers at the Provincial Institute for Puericulture at Madrid on abandoned new-born infants protected by vaccination with B C G before adoption and returned for hospital care between the ages of 1 and 2 years, certain illuminating material has been assembled.

In three infants traces of the inhalation type of gangliopulmonary tuberculosis were found; in two of them, aged 13½ months and 15 months, respectively, only the scars of a healed infection remained; in the third there were evidences of a progressive type of tuberculous bronchopneumonia. It would appear, therefore, that immunization with B C G does not prevent infection, but if one takes into consideration the rarity with which tuberculous lesions are healed at this age one must in justice attribute this protective process to the vaccination.

In three further cases of tuberculous infection of the mesenteric glands, postmortem examination showed healing processes far advanced, in one case, to extensive calcification.

In no instance was concomitant infection in the pulmonary and mesenteric lymph glands observed. Among eighteen autopsies performed on unvaccinated infants with tuberculous lesions, only three showed involvement of the mesenteric glands, while in eighteen of twenty-two autopsies performed on protected subjects, there was definite involvement of these tissues.

The authors feel that these facts confirm their opinion that inoculation with B C G vaccine is the determining cause of the caseation in the mesenteric glands rather than accidental inoculation by ingestion.

With regard to the tuberculin reaction, a positive Mantoux test was elicited in 44 per cent of the vaccinated infants and in 18.7 per cent of the unvaccinated ones. Several clinical histories are included in the monograph to support the contention of Frias and Roldan that the only effective means of immunization with B C G vaccine is by the oral route and that this vaccination is followed by a benign and curable form of tuberculosis of the mesenteric ganglions in which the reaction of the skin is always positive.

AMESSE, Denver.

GAMNA'S AREAS IN SYPHILITIC SPLEEN. G. PATRASSI, Pathologica **23**:266, 1931.

Siderous splenogranulomas (Gamna's areas) were found in great numbers in the spleen of a 5 year old child with congenital syphilis and in the spleen of a 61 year old woman with numerous sclerogummatous lesions.

E. HAAM [ARCH. PATH.].

THE USE OF REPEATED SPINAL PUNCTURES IN COMBINATION WITH ANTISYPHILITIC TREATMENT IN THE CHRONIC ENCEPHALOPATHIES OF CHILDHOOD OF SYPHILITIC ORIGIN. T. VALLEDOR, Bol. Soc. cubana de pediat. **3**:5 (Jan.) 1931.

The term chronic encephalopathies of childhood is used here in the same sense as Brissaud used it, meaning more or less extensive lesions of the encephalon manifesting themselves by very varied symptoms, especially in the psychic and motor spheres, and appearing at birth or in the first years of life. In those of syphilitic origin, repeated spinal punctures proved to be of great value in relieving some of the symptoms, especially headaches, convulsions and spasticity. In almost all of the patients treated, there was a hypertension of the spinal fluid. Arsenicals (neoarsphenamine) were used intravenously (beginning with 5 mg. per kilogram once a week and increasing the dose gradually until 0.01 Gm. per kilogram was used) in conjunction with mercury. At the same time spinal punctures were used every fifteen or twenty days. The results in the three cases described by the author were quite gratifying.

SCHLUTZ, Chicago.

LOEWENSTEIN'S METHOD FOR CULTURING TUBERCLE BACILLI FROM THE BLOOD STREAM. EDERLE and KRIECH, Deutsche med. Wchnschr. **58**:7 (Jan. 1) 1932.

The culturing of tubercle bacilli from the blood stream is a difficult task. Loewenstein claims however, that his method is simple and reliable. Up to date he has examined five thousand cases. Ederle and Kriech repeated Loewenstein's technic in forty-nine cases; thirty-nine of these patients suffered from tuberculosis, five from infectious arthritis and five others from multiple sclerosis. Only four cases gave positive results. Two of the four patients cured had miliary tuberculosis, and the two others pulmonary tuberculosis. The authors therefore believe that this new method is not so reliable nor so simple as one might think from Loewenstein's reports.

KERESZTURI, New York.

Internal Diseases

DIGITALIS DOSAGE IN AURICULAR FIBRILLATION. ERNEST P. BOAS, Am. Heart J. **6**:788 (Aug.) 1931.

This paper pertains primarily to adults, but may be applied to the needs of children. Mention is made of the generally accepted opinion that children require doses of digitalis in excess of those established for adults. In the presence of fever, digitalis is ineffective unless sufficiently large doses are administered. The weight of the patient is no absolute guide to the total dose of digitalis required. In dealing with a patient who has received no digitalis, it does afford a rough preliminary guide. The size of the maintenance dose must be established by actual trial in each case. In general, the greater the original dose required to slow the ventricles, the larger will be the maintenance dose. All rules, at best, are rough guides. Strict individualization and a sufficient amount of the drug to produce the desired effect, irrespective of the size of the dose, are the essence of successful therapy.

BACHMANN, Chicago.

AURICULAR FLUTTER IN A NEWLY BORN INFANT. JAMES G. CARR and WILLIAM MCCLURE. Am. Heart J. **6**:824, 1931.

The authors report a case of auricular flutter in which variations in the fetal heart tones were noted about three weeks before birth. There was some cyanosis

at birth which readily cleared up. The heart rate was 180 with marked arrhythmia at times. No murmurs were heard. The heart rate and rhythm were definitely influenced by deep respiration. An electrocardiogram taken two days after birth was interpreted as a flutter with a 2-1 rhythm. On the tenth day after birth the heart action was normal, with no recurrences of the abnormality.

BACHMANN, Chicago.

DI-HYDRANOL (2-4 DIHYDROXYPHENYL N-HEPTONE) IN THE TREATMENT FOR INFECTIONS WITH INTESTINAL PROTOZOA. HERBERT L. RATCLIFFE, Am. J. Trop. Med. **11**:285 (July) 1931.

The author gives a brief review of the literature on this drug as an intestinal disinfectant and reports a series of experiments with it on both human beings and monkeys. In the human subjects a 25 per cent solution of dihydranol in olive oil was used; in the monkeys a 25 per cent solution was used in some, while agar blocks containing from 0.25 to 0.5 Gm. of dihydranol were used in others. He concluded from his experiments that this drug is highly effective in clearing up infections with pathogenic amebae and ciliates in monkeys and in ridding man and monkeys of intestinal protozoa of lesser importance. In man at least from 60 to 100 capsules (from 9 to 15 Gm.) should be given to be effective. However, much remains to be learned concerning the proper dosage and the best manner of administering the drug.

BURPEE, Augusta, Ga.

ANEMIAS OF INFANCY AND CHILDHOOD. SYDNEY NUSSBAUM, Arch. Pediat. **48**:578 (Sept.) 1931.

This is an interesting and instructive review of the anemia of infancy and childhood. Essential details are given, as well as some of the more recent constructive thoughts in the classification and treatment of anemias of early life. This article cannot be successfully abstracted and should be read in its entirety.

WADDELL, University, Va.

CHRONIC INTERSTITIAL NEPHRITIS IN CHILDREN. RALPH R. SCOBEY, Arch. Pediat. **48**:738 (Nov.) 1931.

A case of chronic interstitial nephritis occurring in a girl 13 years of age is reported. The striking feature of the case is the striking similarity to the picture of chronic nephritis in adults. Arteriosclerosis was present in this case, a rare finding in early life.

WADDELL, University, Va.

MEDIASTINAL EMPHYSEMA. PARKE M. JESSUP, Arch. Surg. **23**:760 (Nov.) 1931.

The author maintains that mediastinal emphysema occurs much more frequently than the available literature leads one to believe. The various ways in which mediastinal emphysema is produced are reviewed. It is generally the result of increased mediastinal pressure which interferes with circulation brought about by the compression of the large veins entering both sides of the heart. In children this condition is noted in injuries to the chest and in resuscitation of the new-born. The symptoms most commonly present are extreme cyanosis and dyspnea, a rapid pulse rate, congestion of the superficial veins of the neck and a low blood pressure. Substernal discomfort and pain may be a complaint; subcutaneous emphysema is usually present, but is not a requisite finding. Physical examination of the chest cannot be depended on. Roentgen observations are not characteristic but are helpful. The author states that all cases of crushing injuries to the chest with a spreading emphysema must be considered as potential cases of mediastinal emphysema. The treatment consists of controlling the source of the air and giving an outlet to the air already accumulated. Various surgical procedures are described that have been of use in treating patients for this serious condition.

KAISER, Rochester, N. Y.

BRONCHIECTASIS IN CHILDREN. GLADYS L. BOYD, Canad. M. A. J. **25**:174 (Aug.) 1931.

The present report is based on the study of fifty-six cases observed at the Hospital for Sick Children, Toronto, during the past ten years. There were twenty-seven boys, twenty-nine girls and three patients whose sex was not specified. The age of onset varied from 2 months to 10 years, most cases, however, starting before age of 2. The following conditions were the factors leading up to the production of the disease: bronchopneumonia, twenty-three cases; recurring or chronic bronchitis, seven; measles and pertussis together, five; pertussis, five; measles, four; influenza, four; empyema, four; tonsillectomy, two; lung abscess, two and cough, two. In the majority not only was the infection mixed, but the flora varied from time to time. Only nine positive responses were obtained in fifty intracutaneous tuberculin tests. No anatomic tuberculous lesions were found among those giving a positive reaction. In twenty-seven of these cases there were demonstrable cavities. In 70 per cent of the unilateral cases the left side was affected. In the six right-sided cases the symptoms were initiated by a tonsillectomy in two instances and by a foreign body in one, whereas on the left side the responsibility was placed on tonsillectomy only once. Of the total series of cases in which abscesses developed, 51 per cent were left-sided and only 27 per cent right-sided. The author discusses the various clinical and physical signs. The use of intrabronchial injections of iodized poppy seed oil 40 per cent has been of distinct advantage in roentgen examinations of the lungs, and few ill effects have occurred. The following tentative plan of treatment has been adopted at the Hospital for Sick Children: bronchoscopic examination following the injection of iodized oil; then (*a*) in unilateral cases, pneumothorax, repeated bronchoscopic suction and postural drainage, and (*b*) in bilateral cases, repeated aspiration, postural drainage and the use of iodized oil.

MOORE, Omaha.

ASCARIS LUMBRICOIDES. A. E. KELLER, J. A. M. A. **97**:1299 (Oct. 31) 1931.

The results of this study show that under environmental conditions unfavorable to the transmission of intestinal parasites the worm burden of infested patients is greatly reduced without the use of anthelmintics. Proper methods of disposal of human feces are more effective in control of the common intestinal parasites than the use of anthelmintics alone.

BONAR, Salt Lake City.

A FAMILIAL EPIDEMIC OF ACUTE GLOMERULONEPHRITIS. A. C. ERNSTENE and G. P. ROBB, J. A. M. A. **97**:1382 (Nov. 7) 1931.

Only a few instances have been reported in which glomerulonephritis has developed simultaneously in several members of a family in close succession. In eight of ten children in one family an acute infection of the upper respiratory tract successively developed, followed by symptoms and signs of acute diffuse glomerulonephritis in six of the children. The time between the onset of the acute infection and the appearance of nephritis supports the hypothesis that this disease results from the development of a state of hypersensitiveness to the primary infection.

BONAR, Salt Lake City.

ADVANTAGES OF INTUBATION METHOD OF INTRODUCING IODIZED OIL FOR BRONCHOGRAPHY IN CHILDREN. S. IGLAUER, J. A. M. A. **97**:1517 (Nov. 21) 1931.

Bronchography has not been generally adopted as a diagnostic aid in children because of the difficulty in obtaining cooperation. The injection of iodized poppy seed oil into the bronchi clearly demonstrates many lesions obscure to ordinary roentgenology. The early diagnosis of pulmonary disease is essential to treatment in nontuberculous infections in children, especially since it is now known that

many chronic pulmonary infections of later life begin in childhood. Intubation is the most practical method for obtaining bronchograms in children.

BONAR, Salt Lake City.

BACTERIOLOGY OF THE BLOOD IN CHRONIC INFECTIOUS ARTHRITIS. H. BERNHARDT and PHILIP S. HENCH, J. Infect. Dis. **49**:489 (Dec.) 1931.

These authors were not able to isolate material of an infectious nature from the blood in most of their cases. In analyzing the literature, they felt that the theory of the infectious nature of chronic arthritis has not been conclusively proved. They state that it is almost impossible to isolate infections from the blood stream with any degree of regularity.

TOOMEY, Cleveland.

TRICHINOSIS FROM THE BARBECUE STAND. CARROLL L. BIRCH, M. Clin. North America **15**:791 (Nov.) 1931.

Birch reports three cases of trichinosis in one family, an adult and two girls, 14 and 11 years old respectively. The probable source was improperly cooked pork eaten at a barbecue stand about nine days prior to examination. The symptoms are divided into three stages, which conform to the stages in the development of the organism: gastro-intestinal, when the adult worms are in the stomach and small intestine; edema of the eyelids — frequently occurring about the eighth day after infection — the cause of which is unknown, but which appears at the time when the embryos are being carried by way of the blood and lymph to the muscles, and muscular pains from invasion of the striated muscles, beginning about the ninth day. The clinical picture varies with the number of the infecting organisms. In the cases of the two children, marked edema of the eyelids without other symptoms was the first indication of the disease. Eosinophilia was present in these cases, reaching as high as 70 per cent. In certain cases it may be possible to find Trichinella in any of the three stages: in the gastro-intestinal contents in the first stage, in the blood (the larvae) during the period of dissemination and in the striated muscle after encystment.

SMITH, Ogden, Utah.

PRIMARY CANCER OF THE THYMUS WITH PLURIGLANDULAR DISTURBANCE. O. LEYTON, H. M. TURNBULL and A. B. BRATTON, J. Path. & Bact. **34**:635, 1931.

Two cases have been described in which carcinoma of the thymus appears to have been associated with pluriglandular disturbance. In a boy, aged 11, fatness of the face, conspicuous hypertrichosis of the face and prominence of the abdomen developed within a month. In a man, aged 31, increasing fatness of the neck and trunk and striae atrophicae on the abdomen developed during less than a year. During the same period, he suffered from night sweats, thirst and polyuria. Both patients, on admission to the hospital, were found to have diabetes mellitus. In both, at necropsy, a small cell medullary carcinoma of the thymus was associated with great hypertrophy of the cortices of the suprarenal bodies, functional hypertrophy of the thyroid gland, infiltration of the medullae of the suprarenal bodies by lymphocytes and plasma cells and fatty infiltration of the centers of the hepatic lobules. Duguid and Kennedy (1930) have described glycosuria, enlargement of the suprarenal bodies and colloid goiter in association with a small cell medullary carcinoma of the thymus in a woman aged 64.

AUTHORS' SUMMARY [ARCH. PATH.].

THE EXCRETION OF CREATININE BY THE HUMAN KIDNEY IN HEALTH AND IN NEPHRITIS. C. L. COPE, Quart. J. Med. **24**:567 (July) 1931.

The author refers to the work of Addis and others relative to the excretion of urea and its relationship to blood urea concentration. He then describes the

method and experimental results obtained from his study of creatinine excretion. He concludes that in the normal subject a linear relation between plasma creatinine concentration and the rate of creatinine excretion exists. The ratio $\frac{\text{mg. of creatinine excreted per hour}}{\text{plasma creatinine, mg. per 100 cc.} - 0.5 \text{ mg.}}$ was found to have a practically constant value of about 125. The 0.5 mg. subtracted represented inert noncreatinine chromogenic substances in plasma. The creatinine-excreting power, as measured by the foregoing ratio, was found to be progressively impaired in nephritis. Creatinine is excreted three times as readily as urea in the normal subject. In the nephritic subject, the author found that the impairment of creatinine excretion approximately paralleled that of urea excretion.

BRADFORD, Rochester, N. Y.

STATUS THYMICOLYMPHATICUS IN LEGAL MEDICINE. W. G. DABROWSKI, Ann. de méd. lég. **11**:128, 1931.

Studies were made of thymic and lymphoid tissue from 920 bodies. When death occurred quickly, whether due to suicide, to other violence or to fulminating disease, the thymus gland and lymphatic tissue were well developed in most young undebilitated persons, and no great difference in the development of those tissues was found in subjects of the same age group. A persistent thymus or so-called status thymicolymphaticus, therefore, cannot be considered proof of a predisposition to sudden death. Indeed, in these observations, proof of status thymicolymphaticus as an innate constitutional characteristic was lacking. Overdeveloped thymic and lymphatic tissue was not found more frequently in suicides than in other bodies when death had occurred quickly.

BARTON, Evanston, Ill. [ARCH. PATH.].

LYMPHANGIOMA OF THE TENDON. R. HUGUENIN and C. OBERLING, Bull. Assoc. franç. p. l'étude du cancer **20**:144, 1931.

Two cases of this disease, which occurred in a boy of 3 and in a man of 47 years, respectively, are well reported.

FRIED, Boston [ARCH. PATH.].

EXOPHTHALMIC GOITER IN A CHILD FOUR AND A HALF YEARS OLD. R. A. MARQUÉZY and JAMMET, Bull. Soc. de pédiat. de Paris **29**:62 (Feb.) 1931.

Exophthalmic goiter in a child, aged 4½ is rare. The patient described had a diffuse thyroid enlargement, more marked on the right side, first noted at the age of 2 years and becoming much more marked in the few weeks preceding this report. There was marked exophthalmos and the eye signs were all positive. The patient had tachycardia (140) but no tremor. There were marked emotional and vasomotor disturbances; she would burst into tears on the slightest provocation, and sweating of the head and thorax, as well as hot flushes, occurred frequently. The blood pressure was raised and the oculocardiac reflex was pronounced. The basal metabolism was practically within normal limits on the three occasions when it was recorded (—8, 10, 12). When the basal metabolism is not raised, some insist that this condition is not true Basedow's disease; they speak of it as a para-Basedow's syndrome due to parasympathetic disturbance, regard thyroid therapy as unnecessary and prescribe sedative treatment. In the present case roentgenologic treatment, consisting of five exposures at intervals of two weeks, was given, with very good results, and it is thought that this was a case of thyroid dysfunction, primary or secondary.

BENJAMIN, Montreal, Canada.

ENORMOUS CARDIAC DILATATION OF UNKNOWN ORIGIN IN AN INFANT FOURTEEN MONTHS OLD. E. APERT, BESSON and BAILLET, Bull. Soc. de pédiat. de Paris **29**:76 (Feb.) 1931.

A boy, 14 months old, presented an enormous cardiac dulness and no other physical signs. He had been normal until the age of 11 months, when he began

to have some dyspnea. This subsided and the child thrived nicely until, at 14 months, he began to lose weight, developed dyspnea, stridor and sternal retraction again and died after a short time. Roentgenologic examination confirmed the marked cardiac dilatation. A complete autopsy was performed. An enormously dilated heart was found, the myocardium was thinner and the lungs showed some areas of atelectasis. The liver, spleen, kidneys and suprarenals were normal. Histologic examination of the various organs, including the heart, showed nothing abnormal except for a slight congestion and edema of the myocardium; there was no evidence of any inflammatory reaction. The exact cause of the idiopathic cardiac dilatation remained undetermined. BENJAMIN, Montreal, Canada.

MEDIASTINAL TUMOR OF SUFFOCATIVE TYPE IN A CHILD SIX YEARS OLD. R. A. MARQUÉZY, A. HERAUX and WILLM, Bull. Soc. de pédiat. de Paris **29**:85 (Feb.) 1931.

A boy, 6 years old, presented the usual symptoms of croup. He was given diphtheria antitoxin, and intubation was performed without relief. He was then examined roentgenologically, as it was realized that he was suffering from tracheal compression rather than from laryngeal diphtheria; he died while undergoing this examination. Except for a mild bronchitis and the exanthemas of childhood, he had been well until five days before his admission to the hospital. His acute illness began then with a dry hacking cough, followed by the onset of dyspnea forty-eight hours later. The dyspnea was moderate until the day of his admission, when it became marked, with stridor and cyanosis; the voice was not affected. Autopsy revealed a tumor of the anterior mediastinum, about the size of the normal adult heart. It pressed on the heart and inner borders of the lungs and reached to the diaphragm, but did not infiltrate any of the surrounding organs. The regional lymph glands were enlarged. No metastases were found. Histologically the growth proved to be a lymphosarcoma. There were no Hassal corpuscles in the sections, but this does not exclude the possibility of the thymic origin of the tumor as these bodies may be lost in the progress of the tumor growth. The authors do not agree with those who would class all such mediastinal tumors as thymogenic, and report this case as one of lymphosarcoma. Because of the absence of any evidence of pleurisy or pericarditis, which usually accompany malignant growths of the mediastinum, the abrupt onset of suffocative symptoms and their rapid progression, causing death, the authors think it advisable to speak of a suffocative type of mediastinal tumor. BENJAMIN, Montreal, Canada.

THE POTASSIUM AND CALCIUM CONTENT OF PLEURAL EFFUSIONS. DUMITRESCO-MANTE and PETROVANO, J. de physiol. et de path. gén. **29**:288 (June) 1931.

In a study of eleven cases, the potassium content of the pleural liquid was variable and in direct relation to the cellular elements, notably the erythrocytes. In the centrifugated liquid the potassium content was much more constant, with a mean value of 22.62 mg. per hundred cubic centimeters. The presence of leukocytes had no influence on this value. The mean value for potassium in whole blood was 193.8 mg. per hundred cubic centimeters and for potassium in the plasma, 26.5 mg. The calcium contents of noncentrifugated and centrifugated pleural fluid were 9.80 and 8.65 mg. per hundred cubic centimeters, respectively, on the average. They showed no relation to the erythrocyte level. The calcium content of the blood was within normal limits. The results suggest that calcium is somewhat less diffusible than potassium through the pleura.

KUGELMASS, New York.

STILL'S DISEASE. R. REITANO, Arch. ital. di anat. e istol. pat. **1**:489, 1930.

The literature on Still's disease is summed up. A case that had lasted three years is described in a girl aged 18 years. Clinically, there was stiffness of the

wrist and sternoclavicular joints. The latter were deformed. The spleen, increased in volume, presented atrophy of the follicles, congestion and hyperplasia of the reticulum cells. The various lymph gland systems were diffusely swollen; histologically they presented partly typical tuberculous lesions, partly slight reduction of the follicles, increase of the reticulum cells, desquamation of the sinuses and hyalinosis of the stroma. In some joints, with macroscopically visible erosions, there were regressive changes in the cartilage, and even necrosis and substitution with fibrous tissues. Tuberculous areas were found in the lungs and liver. The author considers Still's disease as a morbid syndrome of multiple etiology; in the case described there probably existed a tuberculous factor.

G. PATRASSI. [ARCH. PATH.]

LACERATION OF THE LIVER FROM THE PRESSURE OF AN AUTOMOBILE. COLLAPSE FROM HEMORRHAGE. LAPAROTOMY. CURE. MARTINEZ VARGAS, Med. de los niños **32**:193 (July) 1931.

Laceration of the liver with copius hemorrhage, if an operation is not performed immediately, has a mortality of 80 per cent. A case is reported in a boy aged 7 years, in which an automobile passed over the body. The aspect was one of great shock, retching, shallow respiration, a small, rapid pulse, pallor and cold extremities, all denoting serious internal hemorrhage. Palpation revealed a contraction of the abdominal wall muscles especially in the right hypochondriac region, and percussion showed a dulness on the same side extending down to the right iliac fossa. These findings suggested a diagnosis of internal hemorrhage with a probable lesion of the liver. Laparotomy confirmed this diagnosis.

DWYER, Kansas City, Mo.

MARKED PERISTALSIS IN PYLOROSPASM. J. P. GARRAHAN and C. M. PIUTOS, Rev. de especialid. **7**:926 (Oct.) 1931.

Photographs of marked peristalsis in a child of 6 weeks are shown. He gained well, and vomiting ceased after treatment with atropine and feedings of condensed milk.

SANFORD, Chicago.

WATER CONTENT OF BLOOD IN THE PREMATURE INFANT AS RELATED TO PHYSIOLOGIC ANEMIA. GUIDO SANPAOLESI, Jahrb. f. Kinderh. **132**:277 (Aug.) 1931.

The dry weight of whole blood was found to reach a low level at the third month, when "physiologic" anemia was most marked. From this fact, the author assumes that hydremia exists. (He takes no account of the fact that a lowered volume of red cells would, in itself, lessen the dry weight.)

CLAUSEN, Rochester, N. Y.

INFECTION AND REGENERATION IN THE GROWING CHILD. A. O. KARNITZKY, Jahrb. f. Kinderh. **132**:345 (Aug.) 1931.

The author makes a plea for the study of the stage of reparation after infection by quantitative methods.

CLAUSEN, Rochester, N. Y.

CREEPING SUBACUTE PNEUMONIA IN CHILDHOOD. GERTRUD REME, Monatschr. f. Kinderh. **50**:297, 1931.

There is no doubt that an improved technic in roentgenology has greatly aided the diagnosis of pulmonary conditions. However, the author calls attention to a group of cases in which the roentgen observations are typical of tuberculosis. In nine children the history showed a chronic process with a low fever and chronic cough, highly suggestive of tuberculous infection. Roentgenograms confirmed the

diagnosis, and the children were put under treatment. The disease was not tuberculosis, however, as proved by negative tuberculin reactions and a rather speedy recovery. The author reports these cases as falling into a group which for lack of definite symptomatology she calls "creeping (*schleichend*) subacute pneumonia." X-ray pictures are shown.

GERSTLEY, Chicago.

SPONTANEOUS SERUM SICKNESS. VLADIMIR MIKULOWSKI, Monatschr. f. Kinderh. **50**:344, 1931.

The author reviews the symptoms of serum-sickness, and reports two cases of tuberculous infection in children in whom absorption of the serous exudates was followed by symptoms typical of serum sickness, an autogenous serum disease.

GERSTLEY, Chicago.

"GUTTADIAPHOTS" IN CHILDHOOD. OPITZ and KRUGER, Monatschr. f. Kinderh. **50**:377, 1931.

By the term "guttadiaphot" is meant a reaction described by Schilling and his associates, obtained by placing drops of venous blood on strips of colored paper. Three strips are used, red, light green and blue. The paper is then held to the light and interpretations are made by observing the various color effects and rings. At first it was thought that characteristic changes developed in syphilis. Later it was considered that the changes were limited to a certain group of diseases, such as syphilis, tuberculosis and infectious diseases. The authors tried the test in 180 children. They decide that it is entirely unspecific. It may be positive in prematures. In general, it belongs to the same type of reaction as sedimentation of the erythrocytes, but the reactions do not parallel each other.

GERSTLEY, Chicago.

THE FATE OF DIABETIC CHILDREN TREATED WITH INSULIN. M. TRUSEN and E. WALENTA, Monatschr. f. Kinderh. **51**:15 (Sept.) 1931.

Since 1923, 50 diabetic children have been treated at the University of Berlin Children's Clinic. The therapy consisted of insulin given three times daily, starting with doses of 5 units and increasing until the urine became sugar-free. The largest dosage reached was 60 units a day. The diet prescribed contained from 0.3 to 0.5 Gm. of animal protein per kilogram of body weight. The caloric need was then filled with a diet of two-thirds fat and one-third carbohydrate, with plenty of cellulose-containing watery vegetables. At present the authors have a record of 45 children, of whom 24 are living. The geographic distribution of the deaths is worthy of note: (1) Of 15 children from Berlin, 5 died; (2) of 8 children from cities of over 20,000 population, 2 died, and (3) of 22 children from towns of less than 20,000 population, 14 died. The authors conclude that this shows definitely that the present day prognosis in juvenile diabetes depends entirely on the careful supervision of the case. This is obviously more feasible in the larger communities.

GERSTLEY, Chicago.

BLOOD SUGAR CURVES IN ACUTE FEBRILE INFECTIONS. W. SICK, München. med. Wchnschr. **78**:609 (April 10) 1931.

An acute infection usually aggravates, but may improve, an existing diabetes. Sick tried to find some reason for this by studying the sugar tolerance curves in several acute infections: tonsillitis, arthritis, pyelitis, grip, bronchitis and early pneumonia. After a twelve hour fast, two doses of lactose, 30 Gm. each, were given, an hour apart. The blood sugar curves simulated in some respects those found in diabetes. The fasting values were normal. There was a rapid rise in the curve after the first dose of sugar. The second resulted in a still higher peak

suggesting a lack of mobilization of insulin. The curve dropped slowly; after four hours it was still above the fasting level. There was no hypoglycemia. In contrast to diabetes glycosuria did not occur.

BRAHDY, Mount Vernon, N. Y.

ETIOLOGY AND CLINICAL PICTURE OF ACUTE INSUFFICIENCY OF THE SUPRARENAL GLANDS (HEMORRHAGES AND HYPOPLASIA). T. BAUMANN, Ztschr. f. Kinderh. **51**:276, 1931.

The suprarenal insufficiencies in the different periods of life are not to be separated according to organic and age constitution, but according to external influences qualified by age; thus, in the newly born period they are characterized by birth trauma or by stasis in the cava system, in addition to a special organic disposition, while infectious, toxic processes are infrequent. By contrast, in the later periods, infectious processes are frequent and stasis is rare. Acute insufficiency in organic underdevelopment of varied origin is compared with juvenile diabetes mellitus or hypofunction of the islands of Langerhans. One case of calcified suprarenals, one case of hypoplastic cortex of the suprarenals with symptoms of acute insufficiency during the course of a fatal pneumonia and two cases of acute insufficiency from suprarenal apoplexy of septic origin are described.

EMERSON, Boston.

PATHOGENESIS OF ACUTE LEUKEMIAS. R. GROSSER, Ztschr. f. Kinderh. **51**:294, 1931.

The description of transition cases of so-called acute leukemia in which, in spite of completely similar clinical symptoms (hemorrhagic diathesis, ulcerative processes in the mouth, anemia and septic temperature), "myeloid" metaplasias are only indicated or are omitted altogether suggests that this group of diseases is to be regarded as a special reaction to different, apparently septic poisons and not as acute leukemia *sui generis*. All such reactions may represent the picture of a "symptomatic aleukia": thrombopenia, anemia and leukemia with almost complete disappearance of the granulocytes. These are to be differentiated, as primary myelophthises, from Frank's "hemorrhagic aleukia." In questionable cases, which sometimes are diagnosed acute myeloid and lymphatic leukemia and sometimes as "symptomatic aleukia" in sepsis, there are found beside symptoms of injury or irritation of the erythropoietic and megakaryocytic systems those irritations of the granulocytic system called primary irritations. The implication of the lymphatic system, not always present, is secondary, even when there is lymphatic hyperplasia or metaplasia. Evidence for this view is: (*a*) There are transition cases, temporary swelling of the lymph glands and an increase of lymph cells in the bone marrow in acute myeloidosis; (*b*) it is not possible to demonstrate, with irritants, primary lymphotropic activity, which must be assumed etiologically in acute leukemia; (*c*) the so-called "lymphatic reactions" have appeared as called forth by a lymphotropic virus (Pfeiffer's disease or lymphemoid glandular fever) and not as a lymphatic reaction of the body caused constitutionally; (*d*) the cases of acute mixed cell leukemias, which merge with these cases when collections of lymph cells are found in the bone marrow in acute myeloidosis, and cases of myeloid metaplasia in the spleen and lymph glands in acute lymphatic leukemia. The peripheral insufficiency of the blood system against the poison is the cause of the clinical agreement of the forms mentioned and the variations in the pathologico-anatomic changes, on the basis of which the central abnormal reactions develop. As causes of functional inferiority are to be considered constitutional factors, a variation in the degree of sufficiency of the blood system against toxins, a disturbance of an organ regulating the blood system (spleen?) and an abnormal amount of irritation.

EMERSON, Boston.

PECULIAR GENERALIZED FLUCTUATING GLANDULAR SWELLINGS IN A BOY ELEVEN YEARS OLD. O. WIESE, Ztschr. f. Kinderh. **51**:432, 1931.

A boy, aged 11 years, had had scrofula and bone tuberculosis as a small child, but no trace was left. During the past year enlarged glands, up to the size of a small apple, had appeared over the body, symmetrically in the axillae and groins, singly and in groups, but not coalescing. The larger ones were fluctuant. Roentgen examination of the lungs gave negative results, the tuberculin test was negative nine time and tests of the blood were negative. A milky fluid was obtained by puncture; this was not a pure chyle, but porridge-like and chalky, showing under the microscope detritus, some lymphocytes, fat droplets and no bacteria. Three tests done on guinea-pigs were negative. Histologically, an excised gland was made up of extensive caseous foci embedded in fibrous connective tissue poor in nuclei. There was no evidence of a specific inflammation. An animal test gave negative results. The diagnosis seemed to lie between tuberculosis and lymphogranuloma. In the next seven months the boy gained 4 Kg. and no new swellings appeared; he was then lost track of.

EMERSON, Boston.

TWO CASES OF HIGH EOSINOPHILIA. T. INOUYE, J. Pediat. (Tokyo), Dec. 20, 1931, no. 379, p. 1881.

The author reports two cases of eosinophilia of rather high degree. The first patient was a boy of 15 years whose only complaint was a slight daily rise in temperature to 38.5 C. (101.3 F.), and whose tuberculin test was positive. The initial examination of the blood showed a total white count of 31,325 cells per cubic millimeter with 81.9 per cent eosinophils. The total white count and the eosinophil percentage decreased only gradually, but at the end of the third year of observation the count was 8,190 with 27.2 per cent eosinophils. The second case was that of an 8 year old boy whose complaint was also a daily rise in temperature to 39.5 C. (103.1 F.), with a history of an attack of peritonitis three years previously. D'Espine's sign was positive down to the fifth dorsal vertebra, with suppression of breath sounds over the lower lobe of the right lung posteriorly, but with a negative intracutaneous tuberculin test. Examination of the blood revealed the highest white cell count to be 13,237, with 64.2 per cent eosinophils. One year afterward, the total white count was still 13,075, with 25.6 per cent eosinophils. Both of these cases were diagnosed as tuberculosis, but the high white count and high eosinophil percentage in the peripheral blood cannot be explained adequately on the basis of tuberculosis. The author proposes the term "constitutional eosinophila" in a restricted sense, to apply to this condition.

KATO, Chicago.

Nervous Diseases

THE DEHYDRATION METHOD IN EPILEPSY. D. E. CAMERON, Am. J. Psychiat. **11**:123 (July) 1931.

After studying the effect of dehydration on twelve deteriorated and noncooperative patients with advanced cases of epilepsy, Cameron concludes that the method is of little or no value in reducing the convulsions or improving the disposition of the patient. Four of his twelve subjects gave evidence of organic neurologic disorder; two had facial asymmetry, two, unequal pupils. Nine of his series had been having attacks for fourteen years or more. The average daily fluid intake under dehydration as practiced by Cameron was very variable; one patient received 1,300 cc. of fluid daily for the first week. During the second week, five of the seven on whom records were available were taking over 1 liter of fluid a day. Nine patients were followed through to the end of the seventh week. Of these, five had fewer fits than at the beginning of the study, the daily averages falling in each case as follows: In one patient, the number of attacks was reduced from 4 to 1; in another, from 18 to 16; in another, from 45 to 34; in another, from 9

to 7 and in another from 23 to 3. Two showed an increase in the average number of spells (an increase of from 4 to 6, and from 3 to 11) and two showed no change. (The analysis given has been made by the abstractor from the author's tables.) In drawing conclusions from his charts Cameron says that "in some cases the number of fits is increased—in none is there a marked and constant reduction." The procedure was then reversed and fluid was forced. This failed to increase the number of convulsions; but the fluid intake under this regimen was not much in excess of the amount used with dehydration. Cameron admits that many of his patients stole water; some would eat snow, some would steal from other trays; some would drink from the flower vases. In spite of this, and in spite of the small number of patients, in spite of the reduction in the number of fits observed and disregarding the fact that his patients were deteriorated, advanced and admittedly noncooperative, Cameron concludes that the dehydration treatment is of little value in epilepsy.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.].

LAURANCE-BIEDL SYNDROME. WEISS, Endocrinology **15**:435 (Sept.-Oct.) 1931.

In medical literature forty-seven examples of the Laurance-Biedl syndrome have been recorded, the present case being the forty-eighth. All of these resemble each other closely, a distinctive feature being the familial occurrence. They are characterized by a cerebral form of adiposity associated with mental deficiency, adiposogenital dystrophia, retinitis pigmentosa and frequently polydactylism. The child in the case reported was 15 years of age. The development of her symptoms followed an illness at the age of 4 years, during which she had high fever and tremendous retraction of the head, and remained apparently "asleep" for two weeks. Endocrinotherapy caused some loss of weight. JACOBSEN, Buffalo.

THE TREATMENT OF POLIOMYELITIS. JOHN RUHRÄH, J. A. M. A. **97**: 1224 (Oct. 24) 1931.

Treatment for poliomyelitis after the acute period consists of relief from pain, rest and prevention of deformity. Massage and exercise, which may be passive, assisted or voluntary, may be carried out under water, but should always be supervised. Too little treatment of this kind in the first six months is better than too much at any time. An increase in the volume of urine, especially at night, is suggestive of serious fatigue. BONAR, Salt Lake City.

CONVULSIVE MANIFESTATIONS IN HUNTINGTON'S CHOREA. J. NOTKIN, J. Nerv. & Ment. Dis. **74**:149 (Aug.) 1931.

The author reviews the literature and finds convulsive seizures in Huntington's chorea not particularly common. Some nineteen authors have reported instances since 1880. The case of a woman, aged 55, with a family history of alcoholism and mental disease, is discussed by the author. This woman, at the age of 49, became seclusive and apathetic, and indulged in moderate alcoholism; unsteadiness on her feet developed. Dizziness, pains in the head and more marked disturbance of equilibrium followed. Three years prior to commitment, delusions of persecution developed; she became forgetful, and seemed mildly depressed and unstable emotionally. Progressive deterioration set in, with poor orientation, an unstable, dancelike gait and convulsive seizures of a generalized character, with loss of consciousness and somnolence. Speech became indistinct. The study of the pathology of the brain in the literature shows no uniformity of findings. Lesions have been found in the corpus striatum, precentral gyrus, frontal lobe and occasionally in the other cerebral lobes. Many of the unconscious attacks recorded in the literature are not accompanied by motor phenomena. In ten instances the convulsive attack preceded the onset of the chorea, and in six it occurred at the same time. In some cases one finds a history of involuntary movements in various

muscle groups under emotional stress long before frank choreic movements appeared. Convulsive manifestations in other members of the family are recorded frequently enough in the literature to be of great significance, and suggest some relationship between Huntington's chorea and the idiopathic group of convulsive states.

HART, Greenwich, Conn. [ARCH. NEUROL. & PSYCHIAT.]

NEUROLOGIC ASPECTS OF POLIOMYELITIS. CHARLES ROSENBECK, M. J. & Rec. **134**:491 (Nov. 18) 1931.

The author gives some of the differences that existed between the symptoms shown in the present epidemic and in the epidemic of 1916. He gives the preparalytic phenomena of the disease, and groups them under two headings, constitutional and cerebrospinal; he states that one type dominates the picture to the exclusion of the other. The cerebrospinal symptoms are: headache, vomiting, neck and spinal rigidity, the Kernig phenomenon and reflex anomalies. The constitutional signs are: a temperature of from 100 to 103 F., a rapid pulse rate and reddened and edematous fauces. Delirium is rare. The presence of from 20 to several hundred cells in the spinal fluid clinches the diagnosis. The advent of the paralytic stage is in from twenty-four to ninety-six hours. Sequelae of the disease vary according to the distribution and degree of the paralysis.

WILLIAMSON, New Orleans.

THE RÔLE OF PHYSICAL CONDITIONS IN BEHAVIOR PROBLEMS. ARTHUR TIMME, Ment. Hyg. **15**:468 (July) 1931.

The medieval idea that crime and insanity are controllable deviations, deserving of punishment, has not yet entirely disappeared. However, with the advance of pathology and physiology in the nineteenth century, emphasis was placed on behavior disorders associated with physical conditions, such as the irritability of hyperthroidism, the expansiveness of the patient with dementia paralytica and the moria of the patient with a tumor of the frontal lobe. While there is danger of oversimplifying by searching too closely for a simple physical agency, this factor must always be kept in mind. Timme gives two examples: In a boy with hypopituitary obesity the organic defect caused a craving for sweets, and his environment made satisfaction impossible. This child stole change to buy candy and to impress his playmates. Timme also cites the example of a child with a strabismus who, to prevent constant teasing, became a fighter. The fact that these disorders are not simply organic or simply psychogenic, but of a rather complex origin must always be borne in mind. Among the physical defects that frequently give rise to behavior disorders, Timme mentions measles, mumps, malnutrition, chronic infections, orthopedic deformities, encephalitis and endocrine defects. He warns that these factors must not be overemphasized to the point of neglecting the social agencies and environmental problems that may be responsible for the condition. From a properly balanced point of view, the physical condition is considered the starting point, because discrepancies in the social situation, home environment or emotional attitude fail to provide adequate compensatory satisfactions.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

HYDROCEPHALUS SUCCESSFULLY TREATED BY THE USE OF THEOBROMIN SODIO-SALICYLATE. HAROLD T. NESBIT, South. M. J. **24**:1028 (Dec.) 1931.

There are three methods of treatment available for hydrocephalus: (1) operative relief of obstructive types, occasionally with a brilliant result but associated with a high mortality rate; (2) repeated lumbar or cisternal punctures, which usually lead to only temporary improvement, and (3) treatment with theobromine sodio-salicylate. The last-mentioned treatment is sometimes successful, and always warrants a trial.

SCHLUTZ, Chicago.

INFANTILE PARALYSIS. J. E. GONCE, JR., Wisconsin M. J. **30**:813 (Oct.) 1931.

Important considerations are: (1) communicability, (2) an early diagnosis and (3) the early administration of convalescent serum. Infantile paralysis is probably highly contagious because most persons have acquired immunity through subclinical attacks. Where the chance of exposure is greater (in cities) the average age of those contracting the disease is about 5 years, while in rural districts it is about 9 years. Its behavior in this respect is much like that of diphtheria, suggesting a contagion of a similar type. Its transmission apparently occurs in much the same way. The virus is not destroyed by drying or freezing or by the weak antiseptics used in the nose and throat. It is destroyed by pasteurization, sunlight and strong disinfectants. Three types are recognized, the abortive form, which shows indications of a general systemic infection only, and the nonparalytic, with central nervous system signs, which may or may not progress into the third, or paralytic, type. The neurologic signs are less marked than in meningitis, and more careful examination is needed. Definite symptoms and signs should be followed by spinal puncture. An increase in the spinal fluid cells is the most important consideration here. Convalescent serum given intraspinally, intravenously or intramuscularly to a total of from 50 to 60 cc. is indicated in the preparalytic stage. According to the scale used by the Harvard Infantile Paralysis Commission the grade of paralysis in untreated patients is 63.6, whereas in those treated with serum, it is 19. Lumbar puncture for diagnostic purposes is not justified unless serum can be given immediately when the results of tests are positive. This is because the puncture lowers the resistance of the meningeal-choroid plexus and so facilitates the activity of the virus. JANNEY, Milwaukee.

THE AETIOLOGY OF CONVULSIONS. WILFRED EVANS, M. J. Australia **2**:229 (Aug. 22) 1931.

The author reviews the conception of fits as arising from three levels: those arising from the highest level having a distinct aura; those from the middle level being localized or jacksonian and those from the lower level being characterized by tonic contractions; those arising in the cerebellum are characterized by head retraction and opisthotonos. He says that the direct cause is mechanical, vascular or physiocochemical. Mechanical causes includes increased pressure from excessive spinal fluid; vascular causes include marked primary disturbances, and physicochemical causes include the alkalosis of prolonged vomiting, parathyroid disease, etc. Evans also points out that the "convulsive threshold" varies within wide limits. TENNEY, Madison.

CONVULSIONS IN CHILDREN UNDER FIVE YEARS. E. H. M. STEPHEN, M. J. Australia **2**:231 (Aug. 22) 1931.

Convulsions are classified in two groups: (1) intracranial and (2) extracranial. Under intracranial convulsions are lisited: (*a*) those in intracranial hemorrhage of the new-born; (*b*) those in acute intracranial disease, such as meningitis, (*c*) those in chronic intracranial disease, such as tumor, abscess, etc.; (*d*) those occurring in poliencephalitis; (*e*) those due to lead poisoning; (*f*) those due to syphilis, and (*g*) those in intracranial hemorrhage of scurvy. In the extracranial group he includes spasmophilia and the following: (*a*) those due to dentition, (*b*) those due to some digestive disorder of dietary indiscretion, (*c*) those due to worms, (*d*) those which come at the start of some exanthem, (*e*) those due to otitis media or foreign body in the ear, (*f*) those seen in pertussis or pneumonia, (*g*) those which mark the end of a nutritional disturbance, (*h*) those symptomatic of hypoglycemia and (*i*) those due to nephritis. TENNEY, Madison.

CEREBRAL TUMOUR. W. G. WYLLIE, Proc. Roy. Soc. Med. **24**:1185 (July) 1931.

A case of cerebral tumor is reported in a child aged 3 years who had walked normally, but had never talked. The physical and postmortem findings, with a

picture of a section of the brain showing the extent of the tumor, hemorrhagic areas and deformity of the ventricles, are given. WILLIAMSON, New Orleans.

PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY IN A GIRL. E. A. COCKRAYNE, Proc. Roy. Soc. Med. **24**:1343 (Aug.) 1931.

A case of pseudo-hypertrophic muscular dystrophy was reported in a girl 6½ years old. WILLIAMSON, New Orleans.

INTRACRANIAL TUMORS: A CRITICAL REVIEW. F. M. R. WALSHE, Quart. J. Med. **24**:587 (July) 1931.

The author presents an instructive description of tumors of the brain, comprising 50 pages, and a bibliography of 164 references. He discusses the subject under five main headings: (1) Introduction, (2) Classification of Intracranial Tumors, (3) The Etiology of Intracranial Tumor, Trauma, (4) The Symptomatology of Intracranial Tumor, (5) Diagnosis, (6) Treatment and (7) Conclusion. Special stress is placed on the extremely wide pathologic range of these new growths.

BRADFORD, Rochester, N. Y.

CLINICAL TYPES OF MENTAL DEFICIENCY IN YOUNG CHILDREN. CHARLES M'NEIL, Tr. Med.-Chir. Soc. Edinburgh, 1930-1931, p. 166 (in Edinburgh M. J., October, 1931).

M'Neil has taken up the study of the medical and pathologic problems of mental deficiency, supplementing the work of the late Dr. John Thomson, who had studied and recorded 952 cases as abstracted in the AMERICAN JOURNAL OF DISEASES OF CHILDREN (**28**:773 [Dec.] 1924). There were further cases so that the total reached 1,000, and the analysis of M'Neil is based on this carefully diagnosed, rather large block of mental defectives under 5 years of age. Over half of the cases (567) fall under the division of primary amentia, the pathologic cause not known. This contains the large groups of simple primary amentia and mongolism, with a small number of microcephalic aments. The second division, secondary amentia, having a known cause, consisted of 433 cases. The principal cause is birth injury. The number of these cases about equals that of cases of hydrocephalus, epilepsy, cretinism, syphilis and hemiplegia combined, with 50 miscellaneous cases. The figures from these classifications show the great percentage of cases of primary mental deficiency, the large variety of pathologic conditions in the secondary class, and the considerable number of cases of mental deficiency that is not hereditary in origin. It is thus obvious that mental deficiency is not a disease unity, but represents many different conditions in all of which there is the symptom of unsoundness of the mind. M'Neil further classifies the 1,000 cases as to time of origin: antenatal, natal and postnatal. Nearly two-thirds belong in the antenatal group, most of them being of unknown etiology. M'Neill believes that while inheritance does play a part in producing mental deficiency, as for instance in the mating of defectives, the analysis at the clinic shows that a majority are from normal human stock, showing that a good human tree "can bring forth corrupt fruit." The natal and postnatal groups are not the result of vitiated stocks, except in the cases of certain epilepsies. The author emphasizes the fundamental need of medical study and care, which should be linked with the educational and social problems connected with these unfortunate children. NEFF, Kansas City, Mo.

THE ASSOCIATION OF PNEUMOCOCCUS WITH MENINGOCOCCUS IN MENINGITIS. J. CHALIER and A. GUICHARD, Progrès méd., Dec. 26, 1931, p. 2341.

The association of the pneumococcus with meningococcus in meningitis is rare, but has been noted. This association causes a grave prognosis and should be discovered. It is responsible for much of the so-called failure of antimeningococcic serum therapy. SANFORD, Chicago.

MY EXPERIENCES WITH PHENYLETHYLHYDANTOIN IN INFANTILE NEUROPATHOLOGY. P. SUNER, Rev. franç. de pédiat. **7**:540 (Oct.) 1931.

The author reviews the literature on phenylethylhydantoin, and gives his results in four typical cases. He concludes that in repeated doses of 0.50 and 0.60 Gm. a day, there is danger, particularly in case of degeneration or sclerosis of the central nervous system. He obtained somewhat satisfactory results in chorea and epilepsy, but in order to obtain the characteristic exanthem, it was necessary to subject the child to a prolonged hyperpyrexia. It appears to him that in the treatment for epilepsy and chorea minor, it is not good therapeusis to subject a child to a drug that is not without danger.

SANFORD, Chicago.

THE MODIFICATION OF THE SPINAL FLUID CYTOLOGY AFTER LATE EXAMINATION IN VITRO. B. TASSOVATZ, Rev. franç. de pédiat. **7**:638 (Oct.) 1931.

There are two factors involved in spinal fluids *in vitro,* the formation of a reticulation and cytolysis. The reticulation takes place in thirty minutes and reaches a maximum in six hours. Cytolysis begins after six hours and goes on to complete cellular destruction. These actions have a greater effect on the polymorphonuclear forms than on the mononuclears. As a result, there is a diminution in the total number of cells, and a diminution of the percentage of polymorphonuclears, with an apparent increase in the mononuclear elements. In reality, tuberculous meningitis shows a predominance of polymorphonuclears, but by reticulation and cytolysis the formula is inverted and there is an apparent lymphocytosis. The spinal fluid should therefore be examined as soon as it is drawn.

SANFORD, Chicago.

THE POSTENCEPHALITIC MENTAL SYNDROMES. H. STECK, Schweiz. Arch. f. Neurol. u. Psychiat. **27**:137, 1931.

Since the figures are confusing and do not seem to tally well, it is difficult to summarize the statistical data presented in what is otherwise a valuable contribution to knowledge of the mental sequelae of epidemic encephalitis. Steck's inquiry showed that 364 victims of encephalitis had been patients in Swiss asylums for mental disease and that only 14 of these patients had been free from mental symptoms. Parkinsonism was associated with mental disorder in 257 cases. Forty per cent of the patients in the group suffered from bradyphrenia alone or in combination with other psychic disturbances; the remaining 60 per cent showed character changes, as did 63 of a group of 81 patients not afflicted with parkinsonism (77.7 per cent). On the other hand, behavior disturbances were noted in only 20 per cent of 221 cases studied outside the state hospitals. The author has statistics to show that the two principal types of postencephalitic mental disturbance may coexist in the same case, and that either may be seen in persons of all ages, although bradyphrenia is more frequent in older and behavior disorders are more frequent in younger patients.

The author believes that the impertinence and lack of respect displayed by younger patients constitute the psychic counterpart of the hyperactivity and impulsiveness that characterize their general behavior. The hyperactivity and associated irritability is very likely to lead to an explosion whenever an attempt is made to restrain these patients. Their frequent importuning demands, their propensity for teasing as part of a general aggressive tendency, their wheedling obsequiousness combined with a characteristic "sticky attitude" (*"attitude collante"*), all of which may suddenly give way to the grossest impertinence, are commented on. The instincts, particularly the sexual and the food-seeking instincts, are often poorly restrained; exaggeration of the possessive instinct leads to the stealing of unnecessary articles. The behavior of the girls suffering from encephalitis often has an erotic coloring and they show a decided propensity for teasing, while boys, on the other hand, are often brutally aggressive. Previously suggested classifications for behavior disturbances were found unsatisfactory, since indi-

vidual patients often presented symptoms characteristic of two or more of the proposed groups. In general, the prognosis of behavior disorders appears to be bad. Improvement was usually the result of restricted activity imposed by a developing parkinsonism; the essential traits of the altered character remained visible, however, behind the parkinsonian mask. Besides the "sticky affectivity" (*"affectivité collante"*), the author found the irritability, lability of humor, emotional incontinence and "versatility of affect" particularly tenacious. Lability and irritability were the most outstanding characteristics of the emotional disturbances displayed by adults who were suffering from parkinsonism.

In disagreement with Morsier, whose contribution appears in the same number of the *Schweizer Archiv. für Neurologie und Psychiatrie,* the author believes that the postencephalitic behavior disturbances can be differentiated clinically from the endogenous psychoses. These behavior disturbances are essentially organic and resemble personality changes observed in epilepsy and in posttraumatic and postinfectious states. Steck has previously emphasized the *"labilité massive"* and the *"affectivité collante"* displayed by epileptic patients. Hereditary and constitutional factors seem to favor the development of character changes following encephalitis.

The severity of bradyphrenia was not found to be necessarily dependent on the severity of the associated parkinsonism. The author was able to demonstrate in cases of this sort a mental slowing that was some times irregular but always notable. A definite poverty of ideas (*appauvrissement de la pensée*) was indicated by the frequent stereotype and the slight variation of the responses. In some cases, especially when the parkinsonism was severe, the slowing increased as the testing went on, until a state of complete blocking was reached. In spite of the general apathy, as evidenced by the narrowed fields of interest and a frequent indifference in regard to personal affairs, the patients with bradyphrenia generally maintained an affective contact with their families and other persons in their immediate entourage. A rather vapid and dull euphoria was observed now and then, but memory, judgment and orientation remained unimpaired.

The patients suffering from parkinsonism were more subject to fulminating depressive attacks of short duration than to depressions of the endogenous type. The cases in which obsessions and compulsions occurred, though not very numerous, were striking. Phenomena of this sort were associated with respiratory disturbances and other tics in some cases. Oculogyric spasms were often, but not always, accompanied by anxiety states. In the few cases in which epilepsy has followed encephalitis, it has been, in the author's opinion, a matter either of coincidence or of the acute infection acting as a precipitant.

Some of the patients had hallucinations, and a few were paranoid at times, but, in addition, behavior disorders, obsessions, impulsions, oculogyric spasms or other evidence of a preexisting encephalitis were generally present in such cases. Even in cases in which symptoms were the most suggestive of schizophrenia, the *"affectivité collante,"* the absence of true negativism and the conservation of the patient's personality all pointed to the true nature of the malady. These patients, furthermore, generally remained in contact with their environment and showed a more or less critical attitude toward their hallucinations. In a case of real schizophrenia, the symptoms were altered with the advent of parkinsonism to the extent that the clinical picture became more like that of a postencephalitic disorder. Steck believes that the association of schizophrenia with encephalitis may be largely a matter of coincidence.

In conclusion, the author expresses the belief that, in spite of their apparent variability, there is a certain unity in the psychiatric symptoms of the postencephalitic state, a unity assured by the very special coloring of the alterations in behavior. This coloring is based on a "special affectivity." The rarity of dementia in these cases and the close relation of the mental symptoms to the instinctive life of the patient indicate that the mental as well as the neurologic symptoms can be referred to lesions about the third ventricle and aqueduct.

DANIELS, Rochester, Minn. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Ear, Nose and Throat

ACUTE LARYNGEAL OBSTRUCTION IN CHILDREN: CASE REPORTS. CHARLES R. BUGG, South. M. J. **24**:1057 (Dec.) 1931.

The author found that a fairly large number of patients who required intubation did not lose their voice and that in only a few cases was it much changed. No case that the author had the opportunity to observe showed striking unmistakable response to antitoxin before eighteen hours. The antitoxin was given intramuscularly. The patients who were seen in extremis appeared in danger of dying more of circulatory failure than of asphyxia. Marked restlessness and signs of exhaustion are better indications for intubation than signs of obstructive breathing. Children under 2 years of age are more likely to require replacing of the tube after its removal than older children. Only one patient who had breathed easily for eight hours after removal of the tube had dyspnea later. Only one of the patients in the series studied was known to have had toxin-antitoxin, and not any of the patients had had a negative Schick test. SCHLUTZ, Chicago.

OCULAR PALSY: CAUSE. W. G. WYLLIE, Proc. Roy. Soc. Med. **24**:1183 (July) 1931.

A case of ocular palsy was reported in a girl of 4½ years. At the fifth month without fever or headache an ocular palsy developed suddenly. In the right eye there were ptosis and paralysis of the muscles supplied by the third nerve. Whenever the right eye was raised, the left eye turned up and out and showed nystagmus. There were no other neurologic signs. WILLIAMSON, New Orleans.

METALLIC FOREIGN BODIES IN THE BRONCHI AND THEIR SPONTANEOUS EXPULSION. TESONE, Rev. de especialid. **6**:545 (July) 1931.

The author cites two cases, in one of which a child of 5 years, and in the other a child of 8 years, accidentally swallowed a long bodkin and a piece of copper, respectively. Roentgenograms disclosed the objects deep in the lungs, and removal was thought impossible. Both patients expelled them spontaneously in eighteen and fifteen days, respectively. SANFORD, Chicago.

MASTOIDITIS AND THROMBOPHLEBITIS OF THE LATERAL SINUS. C. M. CRISCUOBO, Rev. de especialid. **6**:839 (Sept.) 1931.

The condition occurred in an 8 year old child following otitis media. An operation was performed; postoperative washings with surgical solution of chlorinated soda were carried out, and polyvalent vaccine was given. The child recovered. SANFORD, Chicago.

GIANT CELLS IN THE TONSILS: HISTOPATHOLOGY OF CHANGES IN THE TONSILS DURING THE INCUBATION PERIOD OF MEASLES. W. FINKELDEY, Virchows Arch. f. path. Anat. **281**:323, 1931.

A 7 year old boy had his tonsils removed three days before the appearance of uncomplicated measles. A catarrhal inflammation of the tonsils was found. Histologic examination revealed striking changes in the germ centers. Degeneration and rapid proliferation of the cells were preponderant. In each of the lymph centers about 50 giant cells were found. These contained a surprisingly great number of nuclei. In one section they exceeded 100. Many of the giant cells showed degenerative changes. The specific nature of the pathologic changes in the tonsils was discussed. An allergic reaction of the organism following the infection and a direct action of the toxin were considered as the possible causes of the formation of the giant cells. SCHOENTHAL, New York.

PAPILLOMA OF PALATE: SQUAMOUS CELL EPITHELIOMA OF MUCOUS MEMBRANE OF TONSIL; PAPILLARY CYSTADENOMA OF NASAL VESTIBULE. H. REUYS, Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:167 (Dec. 18) 1931.

Reuys describes three cases of tumor, each of a different type and each presenting an unusual aspect. In the first case there was seen a papilloma of the palate in a girl aged 4 years. The papilloma was of unusual size, being larger than a half dollar. It reappeared quickly after removal with a cold snare, so that the second time a hot snare was used, and the third time removal with a hot snare was followed by cauterization with fuming nitric acid. The last procedure was used for all recurrences thereafter. Histologically, the papilloma was characterized by an extensive and rapid formation of immature connective tissue elements, while mature connective tissue was almost lacking. The author thinks that this fact may explain the frequent and rapid recurrences.

In the second case there was a tumor at the site of the left tonsil in a woman aged 56. The tumor, which was the size of a plum, had a smooth surface. Histologic examination following removal showed a squamous cell epithelioma of the mucous membrane. This case was unusual because the epithelioma had grown slowly without necrosis of the surface, without any macroscopically demonstrable infiltrating growth and without metastasis.

In the third case there was a cystadenoma of the nasal vestibule in a woman aged 47. The tumor was at first diagnosed as a vestibular cyst because of its location, but histologic examination following removal showed that it was a cystadenoma, a type of tumor rarely found in the nose.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TONSILS IN THE PIRIFORM SINUS. C. WIETHE, Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:235 (Dec. 18) 1931.

Wiethe thinks that edema of the larynx may sometimes be traced to a diseased tonsil in the piriform sinus. He supports this hypothesis with the description of a specimen obtained at necropsy in which a tonsil in the piriform sinus and the surrounding tissue showed pathologic changes. The histologic picture was that of a typical tonsillitis. There was profuse cellular infiltration of the tonsillar capsule and adjacent tissues. The blood vessels of the interstitial connective tissue were dilated and congested, especially around the tonsil. From these congested vessels, a submucous edema extended to the arytenoid cartilage. Here the mucous membrane was swollen, the connective tissue fibers were forced apart, and the spaces were filled with a granular mass. This case shows that severe inflammatory processes accompanied by peritonsillar edema may also develop in a tonsil located in the piriform sinus. The author describes a clinical case of this type to show that it may lead to serious consequences. He further remarks that the cellular infiltration observed in the tonsillar capsule and in the surrounding tissue points to the possibility of a phlegmonous process of the larynx originating in a tonsil of the piriform sinus. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

PHONIATRIC STUDIES FOLLOWING TONSILLECTOMY. R. IMHOFER and K. KOHN, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:555 (Oct.) 1931.

Imhofer and Kohn studied the changes in the articulatory organs following tonsillectomy by (1) analyzing the changes in speech developing immediately following tonsillectomy; (2) determining the factors that influence the intensity of the disturbance, and (3) investigating whether tonsillectomy may cause permanent speech disturbances. They state that their technic was comparatively simple. After the tonsils had been carefully inspected and the mobility of the velum palatinum had been determined, certain sound tests were made, and in addition to these auscultation and manometer tests. The studies were made on fifty patients. In twenty-one, articulatory changes were not demonstrable, in spite of the fact that several complained that speaking was painful. This seems to be dependent on the subjective attitude of the individual patient to the pain; some persons avoid

speaking in order to avoid pain, while others feel that they should overcome the pain and strive to articulate plainly. The authors think that the latter attitude is to be recommended. In twenty-eight cases speech disturbances were noticeable, and one case is disregarded because speech disturbances existed already before the operation. In summing up their observations, the authors state that in the majority of cases tonsillectomy is followed by an inhibition in the function of the articulatory organs, which gradually disappears, and that sometimes there even is an improvement compared with the preoperative status. The intensity of the visible reaction and also the degree of impairment detectable with the phoniatric methods of investigation do not always correspond to the speech disturbance; this is due, as already explained, to the attitude toward pain on the part of the individual patient, and it is especially noticeable in the case of the jaws, for the stiffness has no organic cause, and it persists much longer than the impairment of the function of the velum. The authors maintain that as soon as the danger of hemorrhage is over, which at the latest is on the second day following the operation, the articulatory organs may be used for ordinary speaking without resorting to whispering. Phoniatric after-treatment is rarely given following tonsillectomy, and the authors agree that in the majority of cases it is unnecessary.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Skin

THE BLOOD IN PSORIASIS WITH SPECIAL REFERENCE TO CALCIUM, PHOSPHORUS AND POTASSIUM. HENRY MALCOME HEDGE, Arch. Dermat. & Syph. **24**:204 (Aug.) 1931.

The causative factor in psoriasis is a much discussed subject, and the author wishes to show the relation of certain blood elements to the different stages of the disease. He studied specimens of blood from 126 patients with the following determinations of calcium: normal calcium, 67 cases (53.17 per cent); hypocalcemia, 23 cases (18.26 per cent), and hypercalcemia, 36 cases (28.57 per cent). These showed no variation from results in normal persons. The potassium content was found to be normal and to deviate up and down in opposite directions to calcium irregularities. The special groups studied did not show free or ionized calcium and phosphorus to be definitely associated with the cause of psoriasis, but did show that there was evidence of a relationship of this disease to a deficiency of calcium as regulated by the parathyroid hormone. The author feels that the specific plasma protein X, with the combined calcium, should be further studied in the hope of finding a means to stabilize the factor so that it will remain constant.

HENNING, Iowa City.

THE CHOLESTEROL CONTENT OF THE BLOOD SERUM IN YAWS. CHARLES G. AARS and F. O. NIELSEN, Arch. Dermat. & Syph. **24**:418 (Sept.) 1931.

Hypocholesteremia is often met with in syphilis, the lowest values in untreated patients with primary syphilis and the highest, though still subnormal, values in untreated patients with tertiary syphilis. Because of the close relationship between syphilis and frambesia the authors considered it worth while to determine the cholesterol content in patients suffering from the latter disease. The results of the experiments showed that the cholesterol content of the blood serum is low in yaws and that this is of importance for the differential diagnosis of yaws and ulcus tropicum, ulcus simplex and tropical impetigo. Under arsenical treatment, as in syphilis, the cholesterol content increases.

HENNING, Iowa City.

ECZEMA DUE TO FUNGI: REPORT OF A CASE IN AN EIGHTEEN MONTHS OLD BABY. SAMUEL M. PECK and GUSTAV SOLOMON, Arch. Dermat. & Syph. **24**:554 (Oct.) 1931.

The authors report a case in which an original fungus infection of the left hand and both feet occurred with secondary allergic manifestations (epider-

mophytids) over the rest of the body. Trichophytin was applied, and a positive reaction resulted. Fungi were demonstrated microscopically from the large patches of vesiculopustular lesions, which were primary. No fungi were found in the allergic lesions. Whitfield's ointment was applied to the primary lesions with the rapid disappearance of all lesions, both primary and allergic.

HENNING, Iowa City.

LEUKEMIA CUTIS: REPORT OF A CASE. FREDRICK REHM SCHMIDT, Arch. Dermat. & Syph. **24**:587 (Oct.) 1931.

The author reports a rare case of lymphatic leukemia of the skin in a girl aged 2 years. Two discrete, smooth-surfaced nodules, each the size of a hazelnut, were present on the right posterior portion of the neck. They had been present since birth. These lesions were hard and freely movable, and had no connection with the underlying tissue. Their color varied from brown to purple. No palpable adenopathy was present. These nodules were removed and showed lymphocytic infiltration of the cutis layer of the skin. Three months after operation two similar lesions formed on the abdomen and several formed in the old scar. Blood examinations showed a progressive increase in lymphocytes, which were large and of the lymphoblastic type. Deep roentgen therapy helped for a short period, but the patient died six months after admission to the hospital.

HENNING, Iowa City.

A NEW SKIN ERUPTION PRODUCED BY PHENOBARBITAL. M. G. PETERMAN, J. A. M. A. **97**:703 (Sept. 5) 1931.

A severe granulomatous bromoderma of the legs and forearms in a 6 year old boy was apparently caused by the continued use of bromides. Phenobarbital was substituted for the bromides, following which the skin lesions cleared in six months. One week after the dosage of phenobarbital was doubled, identical lesions occurred on both legs and forearms. These disappeared in one month after sodium amytal was substituted for the phenorbarbital.

BONAR, Salt Lake City.

STUDIES IN CONTACT DERMATITIS: I. THE NATURE AND ETIOLOGY OF POLLEN DERMATITIS. AARON BROWN, E. L. MILFORD and A. F. COCA, J. Allergy **2**:301 (July) 1931.

The authors prepared an atopen-free ragweed oil with which they tested 120 persons, divided into three groups: persons subject to ragweed hay fever, those subject to other atopic hypersensitiveness and those without individual or familial atopic history. A dermatitis was produced in 6 members in each group when the pollen oil was applied to the skin by the patch method. The authors classified the dermatitis as one due to contact, similar to that due to poison ivy, sumac and primrose. A description of the method of preparing the oil-free pollen atopen and the atopen-free oil is given.

HOYER, Cincinnati.

INVESTIGATION OF THE MECHANISM OF THE PASSIVE TRANSFER OF SKIN SENSITIZATION. F. E. BECKER and W. C. BLACK, J. Allergy **2**:405 (Sept.) 1931.

A group of experiments were performed with serum from three hypersensitive persons and one who was not hypersensitive. The three hypersensitive persons were sensitive to pasture sage; in addition, one was sensitive to flaxseed and other pollens, another to many pollens and no foods and the third to pollens and foods. The serums from the first two at no time caused sensitization of normal human skin.

The summary and conclusions were as follows: 1. Two of three serums from sage-hypersensitive subjects failed to sensitize the skin to the sage antigen in a

group of twenty-three persons. 2. The refractory serums also failed to produce positive reactions with other antigens to which the donors were hypersensitive. 3. With the positively reacting serum, twenty-two of twenty-three tests were positive, the one exception probably occurring in a person with a refractory skin. 4. Passive transfer may or may not be obtainable with the serums of patients with positive skin reactions and with marked clinical manifestations; also hypersensitive persons who have never had clinical manifestations may give a positive transfer. 5. Passive transfer is not dependent on the degree of skin sensitivity, clinical manifestations, a temporary allergic state or previous desensitization treatment. 6. Passive transfer is not dependent on differences of the blood group of the donor and recipient. 7. The sensitizing factor is not absorbed in vitro by the blood cells from opposite blood groups or by fresh tonsil tissue obtained from nonallergic persons. 8. The leukocytes do not carry a sensitizing factor. 9. Serial injections increase skin sensitization. 10. While failure in passive transfer may be due to a refractory skin as noted by many observers, it seems probable that it may be due, in some instances, to the absence of the sensitizing factor in the donor's serum.

These experiments were all performed on adults.

HOYER, Cincinnati.

STUDIES IN URTICARIA: THE INFLUENCE OF METABOLIC FACTORS. LEO H. CRIEP and LAWRENCE WECHSLER, J. Allergy **2**:479 (Sept.) 1931.

Gastro-intestinal function was studied in forty patients with urticaria. Their ages varied between 10 and 70 years. Eighty per cent showed some type of involvement; one third gave a history of gastric upsets, indigestion and constipation; 21 per cent had hypo-acidity; 23.7 per cent had achylia; 20 per cent showed atony and ptosis; 36.6 per cent showed spasticity of the colon, and 50 per cent some clinical or laboratory evidence of gallbladder disease. The basal metabolic rate was determined in thirty-one patients; in 35 per cent of these there was an increase or decrease in the rate above a normal minus 10 or plus 17. The authors conclude that changes in the gastro-intestinal and thyroid functions are, for the most part, either coexisting with, contributory to or resulting from the urticarial state. They feel that the changes are not sufficiently specific to bear a direct causal relation to urticaria and that the common denominator in these cases is hypersensitiveness.

HOYER, Cincinnati.

PINK DISEASE: ITS MORBID ANATOMY, WITH A NOTE ON TREATMENT. W. G. WYLLIE and R. O. STERN, Arch. Dis. Childhood **6**:137 (June) 1931.

Seven cases of pink disease with observations at autopsy are reported. In all cases the spinal cord showed a diffuse infiltration with small cells which resembled glial cells rather than lymphocytes. Chromatolysis of the central type was found in the anterior horn cells of the cord in five cases. Degenerative changes were found in the peripheral nerves in four cases. In two cases, a slight cellular infiltration was present in the cerebral cortex. No other abnormality in the nervous system was found above the medulla in any of the cases. In the treatment for pink disease, raw liver gave good results.

KELLY, Milwaukee.

AN INQUIRY INTO THE CAUSES OF INFANTILE ECZEMA AND THE RELATION OF BESNIER'S PRURIGO TO THIS CONDITION. GODFREY W. BAMBER, Brit. J. Dermat. **43**:279 (June) 1931.

This paper gives the results of an inquiry undertaken to see how far current ideas and assumptions about the origin of infantile facial eczema and Besnier's prurigo (flexural pruritus, eczema flexuarum and neurodermatitis) could be substantiated by an investigation of the personal and family history of children so affected. The author presents the results of his investigations in three tables, and discusses the points in his inquiry relating to infantile facial eczema in detail under the subheadings: evolution, causation, diet, endocrine imbalance, allergy and

treatment. On the basis of his inquiry, he draws the following conclusions: 1. The high incidence of facial eczema in male infants (3:1) is against an external factor being the chief cause. 2. The initial lesion is either an erythemato-urticarial reaction or a primary pruritus. 3. Fat babies are more likely to be affected. 4. The onset and exacerbations are often associated with gastro-intestinal disturbances and asthma. 5. A family history of an allergic manifestation is not uncommon. 6. Some constitutional peculiarity of the infant is probably the most important factor determining the development of the eczema. 7. Of external factors, cold weather and variations in temperature are the most important. Infection of the skin is neither constant nor necessary. 8. Besnier's prurigo is preceded, immediately or more remotely, by infantile facial eczema in more than half of the cases examined. Transitions from one to the other are seen. 9. The infantile and family history of the children with Besnier's prurigo is similar to that of eczematous infants. The same constitutional peculiarity probably underlies both. WIEN, Chicago. [ARCH. DERMAT. & SYPH.]

ERYTHROEDEMA OR PINK DISEASE. GEORGE WILLCOCKS, Practitioner **128**:78 (Jan.) 1932.

A brief narration of the early history of the disease is given. The author's report covers a study of the records of forty-two cases. He considers as the outstanding signs and symptoms: pink feet and hands, restlessness, irritability, sleeplessness, photophobia, edema of the feet and hypotonia. He states, however, that the only absolutely diagnostic sign is the pink condition of the feet. The duration of the disorder in the series reported varied from three to thirty weeks. As to diagnosis, he stresses the point that it is only the combination of symptoms and signs and their persistence without any discoverable cause that justify the conclusion. The prognosis is serious, particularly in the cases showing complications. When recovery takes place, it is complete. With reference to treatment, a balanced diet is of prime importance. Also, the eradication of any foci of infection should be carefully taken care of. Medication has little place in the treatment except to secure adequate rest for the patient. SAPPINGTON, San Francisco.

THE SKIN AS A PROTECTOR AGAINST LIGHT. HANS MEYER and H. KIRCHHOFF, Deutsche med. Wchnschr. **58**:41 (Jan. 8) 1932.

The skin has two protective mechanisms against excessive ultraviolet irradiation. The short waves of the ultraviolet ray are filtered by the layer of keratin; after excessive treatment by light hyperkeratosis occurs. The longer waves of the ultraviolet rays are filtered by the melanin of the cutis. Melanin has an important rôle as the regulator of the heat rays also. The absorption of ultraviolet rays by different concentrations of melanin solution is demonstrated in the original article by curves. Colorless protein solution has only half as much absorbing power as melanin. When the colorless protein is converted to melanin, the power of absorption is increased. This protective mechanism of the skin against excessive penetration of ultraviolet rays indicates that the good effect of the rays is limited to a certain dosage. KERESZTURI, New York.

MILK-FREE DIET OF INFANTS SUFFERING FROM ECZEMA. R. HESS, Deutsche med. Wchnschr. **58**:52 (Jan. 8) 1932.

Infants suffering from eczema can be fed satisfactorily without milk. Hess advised the use of almond milk in 6 to 10 per cent solution, with the addition of carbohydrates. He has also obtained good results with a whey preparation. Although these feedings can be kept up for months with good results, they should be considered as transitory. Under this regimen the eczema showed definite improvement. KERESZTURI, New York.

THE TREATMENT FOR PSORIASIS IN CHILDREN. EUGEN GALEWSKY, Kinderärztl. Praxis **2**:108 (March) 1931.

After a lengthy consideration of local applications in psoriasis, the author points out the value of roentgen therapy and exposure to sunlight. The prognosis of psoriasis is much better in the case of children than in that of adults.

HUENEKENS, Minneapolis.

DERMATITIS CAUSED BY THE HAIR OF THE CATERPILLAR EUPROCTIS CRYSORRHOEA. D. VAN DER KOOI, Nederl. tijdschr. v. geneesk. **75**:3697 (July 11) 1931.

It is well known that certain caterpillars may cause acute diseases of the skin. Inflammations of the eye caused by the hair of caterpillars are also described (ophthalmia nodosa seu pseudotuberculosa). The author describes a case in which dermatitis, conjunctivitis and a slight inflammation of the cornea developed. It is interesting to know that the inflammation of the eye may develop many weeks after contact with the caterpillar, when the dermatitis has totally disappeared.

VAN CREVELD, Amsterdam, Holland.

Surgery and Orthopedics

ACUTE INTUSSUSCEPTION IN CHILDHOOD. FRANK B. BLOCK and ALEXANDER KOPPEL, Arch. Pediat. **48**:742 (Nov.) 1931.

This study adds nothing to the knowledge of acute intussusception.

WADDELL, University, Va.

THE CAUSE OF DEATH IN ACUTE DIFFUSE PERITONITIS. BERNHARD STEINBERG, Arch. Surg. **23**:145 (July) 1931.

The author endeavored to confirm by experiments on dogs the current conception that toxemia is usually the cause of death in acute diffuse peritonitis. The diphtheria bacillus was used, as it is not found in the intestinal contents. This organism is a definite toxin producer and is capable of producing invariably a fatal diffuse peritonitis in a laboratory animal. It was found that death could be averted by the administration of diphtheria antitoxin. Twenty-two dogs were given intraperitoneal injections of three slants of diphtheria bacilli in 40 cc. of a 2.5 per cent suspension of gum tragacanth and were not given any antitoxin. All of these animals died in from eighteen to forty-eight hours. Fifteen dogs were given similar injections and also 20,000 units of diphtheria antitoxin by different routes. All of the treated animals recovered. The authors noted that the treated animals suffered from intestinal paralysis, intestinal stasis and intestinal bacteria similar to those in the untreated animals, but recovered. Steinberg concluded from the observations under the conditions of these experiments that death is due to the toxin produced by the bacteria present in the peritoneal cavity, and that intestinal paralysis, intestinal stasis and intestinal bacteria play no part in the death of the animal.

KAISER, Rochester, N. Y.

THE UTILITY OF PHENYL-MERCURY-NITRATE AS A DISINFECTANT. L. A. WEED and E. E. ECKER, J. Infect. Dis. **49**:440 (Nov.) 1931.

The authors report favorably on the use of phenyl-mercury-nitrate, stating that the mixture constitutes a safe and practical disinfectant "since it has no odor, color, taste or corroding capacities and does not stain." Not the least interesting part of the report is the statement that the disinfectant when given internally to animals did not produce untoward results.

TOOMEY, Cleveland.

THE BARIUM SULPHATE ENEMA IN THE INTUSSUSCEPTION OF INFANCY. CHARLES LEFRANÇOIS, Union méd. du Canada **60**:453 (July) 1931.

Lefrançois advocates the use of the barium sulphate enema under fluoroscopic control to aid in making an early diagnosis of intussusception. He points out that this diagnostic method alone may result in relief of the acute condition, and if the barium sulphate fails to pass the obstruction the surgeon has gained information as to the best site for making his incision in order to reach the invaginated intestine, thus shortening the time of operation and reducing to a minimum the handling of the abdominal contents. The author states that the use of the barium sulphate enema is harmless, and it will make the diagnosis positive in doubtful cases. The earlier these patients are operated on the better is the chance for recovery, and this method will allow the diagnosis to be established without delay.

TURNER, Chicago.

PERINEPHRIC ABSCESS IN AN INFANT. B. R. MESSINA, Arch. argent. de pediat. **2**:69 (Feb.) 1931.

The author describes a case of perinephric abscess in an infant, 1½ months of age, that is interesting because of the extremely young age of the patient. The illness began with fever, vomiting, diarrhea, coryza, pharyngitis and cough one month before the patient's admission to the hospital. At examination a tumor mass, edema of the abdominal wall, pain and venous engorgement were observed. By means of a puncture green pus was obtained, in which staphylococci and streptococci were found on culture. Operation revealed the presence of a unilocular, extracapsular, retrorenal abscess, which was opened and drained. Recovery followed. The etiology of the abscess was obscure. The author believes, however, that the infection of the upper respiratory tract may be considered as an important factor in its formation.

SCHLUTZ, Chicago.

AN OSTEOBLASTIC SARCOMA OF THE HEAD OF THE PANCREAS. R. C. AGUIRRE, R. BRACHETTO BRIAN and E. J. SAUBIDET, Arch. argent. de pediat. **2**:118 (March) 1931.

The authors report a case of an osteoblastic sarcoma of the head of the pancreas which, to their knowledge, is the only case of that kind reported in medical literature. The patient was a boy, 13 years old, who had a midthigh amputation because of a tumor of the lower left femoral epiphysis, diagnosed as an osteoblastic sarcoma. He was readmitted to the hospital six months later because of nausea and vomiting, epigastric pain, jaundice, clay-colored stools and cachexia of two weeks' duration. Physical examination revealed a marked generalized icterus, an enlarged but smooth liver and a readily palpable gallbladder. A laparotomy was done and ended fatally a few days later. It revealed a markedly distended, smooth gallbladder (13 by 5 cm. in diameter) and a tumor at the head of the pancreas. Necropsy revealed a smooth liver, free from tumor masses, and a gallbladder without inflammatory changes. There was a hard osseous tumor, the size and aspect of an adult femoral epiphysis, involving the head of the pancreas, the adjacent duodenal portion and the common duct. Macroscopic and microscopic examination of the tumor revealed its resemblance to that of spongy bone. The authors consider this tumor to be a metastasis from the tumor of the femur. They believe that, unlike the usual sarcomatous metastasis, it spread along the aortic lymphatic chain and then in a retrograde manner along the superior mesenteric and pancreatic chain of lymphatics.

SCHLUTZ, Chicago.

OVARIAN CYST WITH A TWISTED PEDICLE. J. M. MACERA, B. MESSINA and M. DE LA FARE, Arch. argent. de pediat. **2**:127 (March) 1931.

A girl, 11 years of age, was admitted to the hospital with a severe pain of three days' duration in the left lower abdominal quadrant. A tender mass the size of a

fetal head could be palpated in the left inguino-abdominal region. It was punctured and blood was obtained from it. At operation, a cystic tumor, 13 by 9 by 7 cm., with a twisted pedicle was removed. Pathologic examination revealed a cystic dermoid tumor which, according to the author, is of rare incidence in Argentinian children.

SCHLUTZ, Chicago.

TREATMENT FOR EMPYEMA IN CHILDREN. MARTINEZ VARGAS, Med. de los niños **32**:161 (June) 1931.

Thoracotomy with rib resection is the method of choice in the treatment for empyema. In a case of serofibrinous pleural effusion the author advises aspiration of the fluid and the injection of 5 cc. under the skin. This autoserum therapy facilitates resorption and gives excellent results. Where there is frank pus and no encystment, the fluid should be removed as soon as possible. In a child under 1 year of age a thoracotomy without rib resection is done, and a metal cannula is used to prevent closure of the wound. The fluid should be released slowly, so that the heart if displaced will return to its normal position without violence. Irrigation of the pleural cavity with surgical solution of chlorinated soda dissolves the fibrin and promotes drainage. The instillation of a few drops of colloidal silver or silver protein stimulates cicatrization.

DWYER, Kansas City, Mo.

THE PYELOGRAPHIC DIAGNOSIS OF HYDATID CYST OF THE KIDNEY. L. A. SURRACO and H. MEZZERA, Rev. med. de Buenos Aires **16**:1453 (July) 1931.

The authors give fourteen excellent photographs to illustrate their points. The characteristic sign is a regular, rounded shadow in intimate contact with the calices of the kidney; when the cavity is complete, the regular contour can easily be determined. The best prognosis is afforded by a rupture into the genito-urinary tract; this can be foretold by the position of the calices at the base of the shadow. This is called the "signe de coupe," and is pathognomonic.

SANFORD, Chicago.

EXPERIMENTAL AND CLINICAL STUDIES OF CRYPTORCHIDISM. H. F. O. HABERLAND, Arch. f. klin. Chir. **163**:603, 1931.

In experimental animals it was found that atrophy of the testicles was not due to intra-abdominal pressure, but rather to pressure caused by proliferation of the connective tissue in the canaliculi of the testicles. Malignant degeneration of undescended testicles occurs rarely. It is possible that an undescended testicle may descend spontaneously at puberty. Hormone preparations should be tried to bring about a better development of the sexual organs with a spontaneous descent in view. A phimosis should be corrected so as to allow for a better development of the penis, which may have some relationship to the development of the testicles. An operation should be performed if the inguinal canal is narrow and if it causes pressure on the testicle with its resultant pressure atrophy. If this procedure produces a hernia, it can be repaired later.

KOHN, Milwaukee.

ACUTE PURULENT INFLAMMATION OF THE KNEE JOINT IN INFANCY. H. MAY, Arch. f. klin. Chir. **165**:110, 1931.

Purulent infections of the knee joint in infants are not as rare as they are thought to be. With direct trauma excluded, they are found as a metastatic focus after angina, otitis media, bronchitis, typhoid, etc. The infection is usually located where the vessels of the epiphysis and the metaphysis enter the joint. It may break into the periarticular tissue or into the joint itself. The focal process is always just adjacent to the capsule and just between the cartilage and the bone. Staphylococci, streptococci and pneumococci are most commonly found. The staphylococcic infection is most violent, and causes destruction of the cartilage.

The outcome of this infection is severe in spite of early diagnosis and treatment, and ankylosis often occurs. The streptococcic and pneumococcal infections are less severe, subsequent repair taking place more rapidly. KOHN, Milwaukee.

THE TREATMENT FOR EMPYEMA IN CHILDHOOD. R. NISSEN, Ergebn. d. inn. Med. u. Kinderh. **39**:143, 1931.

The author asserts that all methods of treating children for empyema that cause an open communication between the outside and the empyema cavity lead, in most cases, to the serious consequences that result from open pneumothorax. The danger lies in a shifting of the mediastinum, which has a deleterious influence on the circulation in the vena cava and on the filling and emptying of the right side of the heart. The underlying principle, therefore, of all methods of treatment consists in maintaining as complete closure of the thorax for as long a period as possible. Whenever the pus causes severe toxic or septic phenomena and whenever the exudate is so extensive that it causes undue pressure on the mediastinum and its contents, a paracentesis should be performed in the seventh interspace, at the posterior axillary line. During the first puncture, only part of the exudate should be removed, and not too great a pneumothorax left behind. Subsequent daily punctures are made as long as the fluid is of a proper consistency, and these may be followed by lavage with a solution of ethylhydrocupreine or instillations of a pepsin-boric acid mixture (according to Bier). In staphylococcic empyema fibrin is formed earlier and is of a greater quantity than in empyema due to streptococci. It is for this reason that, as a general rule, streptococcic empyema clears up with punctures alone, whereas in the staphylococcic infections more radical measures must often be resorted to. In infants and children under 2 years of age who tolerate continuous drainage poorly, one may thin down the exudate by injecting a few cubic centimeters of a pepsin-hydrochloric acid solution (according to Herrmannsdorfer). If continuous drainage becomes necessary, it is best—if at all possible—to wait from ten to fourteen days after the pus forms before operation is undertaken; this period gives the mediastinum a chance to become somewhat fixed. The patient with tuberculous empyema should practically never be operated on; he should be treated by repeated paracenteses. CAPPER, Philadelphia.

GENESIS OF COXA VARA. H. HILGENREINER, Med. Klin. **27**:159 (Jan. 30); 200 (Feb. 6) 1931.

Besides the process known under the name of Calvé-Legg-Perthes' disease of the hip joint, which is characterized by destruction of the epiphysis of the head of the femur, there is another analogous destructive process in the region of the neck of the femur. The condition is often found in children of the adiposogenital type, and therefore it is probable that the cause is endocrine dysfunction. Osteochondritis of the neck of the femur is, as a rule, found in early childhood, leads to coxa vara at this age and is therefore also called coxa vara infantum. The treatment is conservative and consists of adequate orthopedic measures, but the possibility of endocrine dysfunction has to be considered and in the future hormonal treatment may bring good results. ZENTAY, St. Louis.

A SPECIAL FORM OF JUVENILE POSTHITIS. KURT OCHSENIUS, Monatschr. f. Kinderh. **50**:255 (July) 1931.

On the prepuce of small boys one frequently finds inflammation and small ulcers which lead to discomfort and even to painful urination. Boys 1 and 2 years of age seem especially predisposed to this condition. As it usually appears with the onset of cold weather, the author thinks that the change to heavier clothing may be responsible. He believes that wool is the exciting factor, as he has found woolen threads in the small ulcers. The treatment is a change to cotton or linen garments.

GERSTLEY, Chicago.

HEMATURIA AND APPENDICITIS. S. WOLFF, Ztschr. f. Kinderh. **51**:662, 1931.

A boy 10 years old, who was up on the tenth day after appendectomy, showed blood and casts in the urine on the eleventh day; this condition cleared up in eight days. Four days after appendectomy, a girl 5 years old showed hematuria for two days. There are fifteen similar cases in the literature. The possible causes may be adhesions between the appendix and the urinary tract, a toxic action, embolism or thrombosis, congestion or nephritis, as revealed by the urinary sediment and autopsy.

EMERSON, Boston.

EMPYEMA IN CHILDREN. M. MIKULA, Časop. lék. česk. **68**:1297 (Sept. 20); 1341 (Sept. 27) 1929.

A review of the literature is followed by a description of the radical and conservative treatments for empyema. Empyema is regarded as of grave prognosis in infants under 3 years of age. A differential diagnosis of empyema and pulmonary abscess is impossible in some cases. In the author's series of 165 cases, 18 patients were under 1 year of age, 79 were from 1 to 3 years old and 78 were over 3 years of age. Before 1927, the death rate was 28.3 per cent for patients operated on under general anesthesia; since 1927, it has been lowered to 8.8 per cent under local anesthesia. In the pneumococcus cases ethylhydrocupreine was used. The tendency is toward conservative treatment in infancy, because the results with pleurotomy have not been gratifying in the early age group. A plea is made for early diagnosis and hospitalization; home treatment, even though conservative, is recommended only for convalescent cases. STULIK, Chicago.

PROGRESS IN ORTHOPEDICS IN THE TREATMENT FOR PARALYSIS AND ANTERIOR POLIOMYELITIS. JANIK ALFRED, Pediat. polska **10**:34 (Jan.-Feb.) 1930.

The author divides the treatment into three stages: (1) acute illness, (2) convalescence and (3) permanent paralysis. He stresses transplantations of muscles and tendons, and gives most of the important principles of this delicate operation.

KRUPINSKI, Chicago.

THE TREATMENT OF BURNS WITH A FRESHLY PREPARED SOLUTION OF TANNIC ACID. J. H. VAN DER SPEK, Nederl. tijdschr. v. geneesk. **75**:873 (Feb. 21) 1931.

The author obtained good results with the method of Davidson (1925) in the treatment for burns. He used a freshly prepared watery solution of tannic acid (5 per cent). It is important that the patient does not receive any other treatment previously. In any case, the patient is first given an injection of morphine (e. g., a child of 6 years was given 7.5 mg). VAN CREVELD, Amsterdam, Holland.

Miscellaneous

ISOLATED GIANT GROWTH OF A BRANCH OF THE PULMONARY ARTERY ASSOCIATED WITH CONGENITAL BRONCHIECTASIS. SOL ROY ROSENTHAL, Arch. Path. **12**:387 (Sept.) 1931.

At autopsy performed on a man 69 years of age, dying of carcinoma of the penis, an excessive overgrowth of a branch of the left pulmonary artery was found. The artery communicated with the pulmonary artery and ended blindly in the subpleural region of the left pulmonary lower lobe. The giant vessel was determined to have originated in a persistent branch of the postbronchial arterial plexus. An accompanying bronchiectasis resulted from pressure on the adjacent alveoli.

LESLIE, Evanston, Ill.

HIRSCHSPRUNG'S DISEASE TREATED BY LUMBAR SYMPATHECTOMY. T. WOOD CLARKE and FREDERICK M. MILLER, Arch. Pediat. **48**:553 (Sept.) 1931.

The authors review the various theories concerning the nature of this condition and review the pioneer studies concerning the relationship of the sympathetic nervous system to intestinal peristalsis and to Hirschsprung's disease in particular. They report in detail one case in which the patient was apparently cured by lumbar sympathectomy.

WADDELL, University, Va.

ABDOMINAL PAIN IN CHILDREN WITH UPPER RESPIRATORY INFECTIONS. RALPH R. SCOBEY, Arch. Pediat. **48**:602 (Sept.) 1931.

The author discusses abdominal pain as a secondary manifestation of infections of the upper respiratory tract, and reports several cases that he thinks were of this nature. Attention is called to the fact that appendicitis appears to occur more frequently during epidemics of infections of the upper respiratory tract. The author states that it is much safer to operate for a possible appendicitis than to "procrastinate and be sorry."

WADDELL, University, Va.

SCHICK TEST MODIFICATION WITH DIPHTHERIA TOXOID. ALBERT V. STOESSER, Arch. Pediat. **48**:607 (Sept.) 1931.

Of seventy-four children with a positive Schick test, forty-six failed to respond to an injection of diphtheria toxoid with a positive reaction. The author concludes that toxoid is not a reliable product to use in the place of toxin-antitoxin in Park's modification of the Schick test.

WADDELL, University, Va.

THE ETIOLOGY OF DENTAL CARIES. ALFRED F. HESS and HAROLD ABRAMSON, Dental Cosmos **73**:849 (Sept.) 1931.

Two groups of children who had been closely observed during infancy (some six or seven years ago) were recently examined for the presence of dental caries. The one group was known to have been free from rickets, as judged by repeated clinical and roentgenographic examinations; the other group had rickets in mild or moderate form during the first year of life. It was found that the children who had been protected from rickets had developed less caries than those who had not been protected. Nevertheless, numerous instances of dental caries were found in the nonrachitic group. The deciduous teeth as well as the first molars were involved. Considerable caries was likewise observed in the teeth of a group of children who had been breast fed and had shown no evidence of rickets in a study carried out in 1922 and 1924. An average degree of caries was found in the teeth of children whose mothers were given cod liver oil during the latter months of pregnancy; this group likewise had been studied for rickets about seven years ago.

A consideration of the geographic distribution of dental caries brought out the fact that it is rampant among the children and adults in the subtropics and tropics, for example, Florida, Hawaii, Jamaica and Trinidad. This distribution constitutes a strong argument against regarding rickets as the essential etiologic factor of dental caries.

A similar consideration of geographic distribution argues against the acceptance of scurvy as an important causal factor of caries, which is present in marked degree where fruit and vegetables are in greatest abundance and, on the other hand, is least prevalent in countries, such as Alaska and Greenland, where antiscorbutic foods are scarce.

An analysis of clinical conditions likewise indicates that dental caries cannot be attributed to a deficiency of vitamins A or B.

Pathologic lesions of the enamel are by no means infrequent among young children. This is a disorder quite distinct from caries and involves particularly the upper incisor teeth. It is found in the deciduous teeth of children who had

neither rickets nor scurvy. As shown by others, there is often an association between this disorder, infantile tetany and a deficiency of calcium in the blood.

A relationship exists between growth and the occurrence of caries and more particularly between development and caries. This is clearly brought out by plotting a curve of incidence of caries and noting the exceptionally high incidence at the period of adolescence and the years immediately succeeding.

AUTHORS' SUMMARY.

ON VACCINE THERAPY AND IMMUNIZATION IN VITRO. ALMROTH WRIGHT, Lancet **2**:225 (Aug. 1) 1931.

The author discusses in turn chemotherapy, the principles of vaccine therapy, the opsonic index and phagocytosis. In conclusion, he questions whether the general acceptance of the idea that homologous vaccine gives the best immunizing response may not be open to exception. It might be open to a general exception if the heterologous vaccine in question were, as compared with the homologous vaccine, more easily soluble in the blood fluids. It might be open to an individual exception if the patient's blood exerted less lytic action on a vaccine made with the infecting microbe than it did on a vaccine made from another microbe.

LANGMANN, New York.

ROENTGENOGRAM OF HYPERTROPHIED THYMUS WITHOUT ANATOMIC HYPERTROPHY. E. LESNÉ, A. RICHARD and J. A. LIÈVRE, Bull. Soc. de pédiat. de Paris **29**:96 (Feb.) 1931.

A boy, 6 months old, swallowed a brooch. He was a normal baby, well developed and well nourished. In the course of roentgen examination a wide shadow in the thorax was diagnosed as due to a hypertrophied thymus. Three days after a gastrostomy for the removal of the foreign body from the stomach, the infant suddenly became very pale, the temperature rose and the child soon died, supposedly of status thymicolymphaticus. At autopsy the thymus was found to be normal as were all the other organs. The thoracic contents were removed intact and roentgenograms were made of these before and after the removal of the thymus. One could hardly discern the shadow cast by the thymus. That seen in the film taken during life must have been caused by dilated vessels. The authors believe that so-called thymic death could often be shown to be due to other causes if these were assiduously sought for.

BENJAMIN, Montreal, Canada.

B C G IN SÃO PAULO (BRAZIL) AT THE CLEMENTE FERREIRA DISPENSARY. CLEMENTE FERREIRA, Bull. Soc. de pédiat. de Paris **29**:104 (Feb.) 1931.

Several hundred subjects, including infants, children and adults, were given immunization courses of B C G, some by mouth and some subcutaneously. The morbidity and mortality figures for tuberculosis are lower for the persons who received B C G than for those who did not.

BENJAMIN, Montreal, Canada.

LARGE COLLECTIONS OF MILK FOR INFANT FEEDING. MARC FOUASSIER, Presse méd. **39**:1187 (Aug. 8) 1931.

For the pasteurization of milk in large quantities Fouassier believes that milk placed in the Soxhlet apparatus may be considered as pasteurized when the water in the container boils. Heating for three minutes at 85 C. is sufficient; longer sterilization is not only useless but undesirable, as the sugar in the milk may be caramelized by prolonged heating. Milk so pasteurized is perfectly safe for infant feeding.

BIEKER, St. Petersburg, Fla.

THE ADMINISTRATION OF SCHOOL HYGIENE. Bol. Inst. internac. am. de protec. a la infancia **5**:1 (July) 1931.

This article is a compilation of opinions obtained from authorities throughout the different countries of North and South America, as to whether the health of the school child should be cared for through the Department of Health or the Board of Education. No definite conclusions are presented.

LESLIE, Evanston, Ill.

STILLBIRTH AND INFANT MORTALITY IN BAHIA, BRAZIL. Bol. Inst. internac. am. de protec. a la infancia **5**:84 (July) 1931.

On account of the high proportion of stillbirths and infant mortality, a serious problem exists in Brazil, to be solved by the government and the sanitary authorities by means of a careful study of its causes and preventive measures. One of the chief points to be considered in this campaign is birth registrations, which should be carried out with the greatest accuracy. The Secretary of Health and Public Service established the sanitary registry to supply the deficiencies of civil registration. The following were the general findings in Bahia: Digestive diseases prevail as a cause of death among infants under 1 year of age, being attributed to inadequate nourishment due to ignorance and inexperience; the social factors of stillbirth and infant mortality are in intimate relation with the medical factors. The Child Health Service of Bahia engages in a double prophylactic and educational task, by means of its clinics, its maternal and child health centers, its "crèche," its "milk-kitchen," its visiting nurses and its "Little Mother" courses for teaching child health in the primary schools. AUTHOR'S SUMMARY.

EDUCATION OF DEFECTIVE CHILDREN. MARIA MARTA VILLALBA OLIVA, Bol. Inst. internac. am. de protec. a la infancia **5**:120 (July) 1931.

Defectives are patients in need of a special education; they should not be kept in ordinary classes because they injure normal children. It is necessary to establish special schools or sections that work in the country or out-of-doors, so as to promote the physical improvement of the weak. Such schools should be maintained by the government, and their budget should include items for school lunches and the school wardrobe. Special schools should be in touch with the common school, but without losing their autonomy. All children suspected of defect should be sent to the special school for examination, and, to this end, such schools should be provided with an experimental laboratory for the school or specialized physicians to work in. Defective children should have the best teachers with special training, and education should develop their minds to make them useful social elements. AUTHOR'S SUMMARY.

CHILDREN'S INSTITUTIONS: THEIR PRESENT STATUS IN AMERICA. C. H. LE BLOND, Bol. Inst. internac. am. de protec. a la infancia **5**:142 (July) 1931.

Institutions for dependent children should provide intensive treatment during a relatively short period; this treatment should include intensive care of the health, education, discipline, recreation and religion. The institution should provide the necessary means to study and understand the child, direct his development, place him in a home, and supervise him until his permanent adaptation is achieved. As a substitute for his natural home, the institution should maintain the child and educate him morally and intellectually. It should employ the principles of good social service, securing the opportunity for mental, moral and physical development, so as to enable the child to become courageous, capable, independent, healthy and happy. AUTHOR'S SUMMARY.

FOREIGN BODY IN THE DIGESTIVE TRACT OF AN EIGHT MONTHS OLD INFANT. WALTER PIAGGO GARZON, Med. de los niños **32**:134 (May) 1931.

An infant swallowed a gold breast-pin. There were no symptoms of mechanical obstruction, no dysphagia, dyspnea or pain. On the following day the temperature rose to 103.5 F., where it remained for three days, but no abdominal rigidity, tenderness or tumor was felt. Roentgenograms revealed the foreign body in the stomach. It passed from the bowel in ninety-six hours, no laxatives or other medication having been administered. The fever was probably a coincidence and due to a transitory digestive disturbance.

In children over 2 years of age, tincture of belladonna has some beneficial action in relaxing a spasm of the intestinal walls, cardiospasm, pylorospasm or spasm in the pharynx or at the ileocecal valve, thereby permitting the passage of foreign bodies. It is given in doses of 5 drops for each year: from 30 to 40 drops to a child aged 3 or 4 years. In the majority of cases foreign bodies with smooth edges can be traced in their course through the bowel and are eliminated naturally without injury.

DWYER, Kansas City, Mo.

B C G VACCINATION AND THE LÜBECK DISASTER. ALBERTI ASCOLLI, Deutsche med. Wchnschr. **56**:1160 (July 11) 1930.

Ascolli inoculated 10,000 hogs with B C G, and found that the vaccine not only was harmless, but also increased the resistance of the animals to tuberculosis. He believes that there is no other reason to explain the Lübeck disaster than as the error of mixing the B C G culture with a virulent human strain. He further suggests the organization of an international B C G league for the study and control of vaccination.

KERESZTURI, New York.

FISTULA FORMATION AFTER EMPYEMA. SUSANNE SEYFFARTH, Monatschr. f. Kinderh. **51**:22 (Sept.) 1931.

The author reports a series of cases of ordinary empyema in which there was a great delay in the closing of the drainage wound. Cultures of the pus disclosed a mixed infection in which the tubercle bacillus played a part. She advocates the idea that such a mixed infection may be responsible for a delayed healing of many empyema wounds in which tuberculosis has never been suspected.

GERSTLEY, Chicago.

TUBERCLE BACILLEMIA IN VARIOUS DISEASES. E. LOEWENSTEIN, München. med. Wchnschr. **78**:261 (Feb. 13) 1931.

Blood cultures for tubercle bacilli in the diagnosis and prognosis of tuberculosis are superior to sputum examinations and physical diagnosis. Cases in which tuberculosis was not suspected showed positive blood cultures. Five patients with a slight increase in temperature but no evidence of tuberculosis in physical or roentgen examination had tuberculous bacillemia. The later course proved the diagnosis of tuberculosis (pulmonary) correct. Tuberculous bacillemia may be present without fever. Some patients with cavity formation who had no fever or bacilli in the sputum and who felt relatively well had bacilli in the blood. This is considered an important prognostic observation. Tests on blood specimens made without the knowledge of the diagnosis (gonorrhea, syphilis, psoriasis, carcinoma) gave negative results. As previously reported, tuberculous bacillemia was found in tuberculosis of the skin and genito-urinary tract. Positive cultures were obtained in twenty-two of twenty-seven cases of acute polyarthritis, which ordinarily is considered rheumatic infection.

BRAHDY, Mount Vernon, N. Y.

VACCINATION AGAINST TUBERCULOSIS. K. RUPILIUS, München. med. Wchnschr. **78**:263 (Feb. 13) 1931.

The oral administration of B C G was found to be inaccurate and unreliable. Parenteral vaccination in man and animals produced tuberculous changes which receded spontaneously. This could be avoided by the use of very small doses of B G G (from 0.0005 to 0.01 mg.) at intervals of a few days. By this method allergy was produced in patients and animals. The animals were immune to experimental infection with tubercle bacilli for the period of a year. The author tested a proprietary ointment marketed for use in protecting infants against tuberculosis. Neither allergy nor immunity was obtained in guinea-pigs with this preparation.

BRAHDY, Mount Vernon, N. Y.

A PRACTICAL IMPROVEMENT OF THE TUBERCULIN SKIN TEST. F. HAMBURGER, München. med. Wchnschr. **78**:577 (April 3) 1931.

The tuberculin ointment introduced by Wallgren for the cutaneous skin test for tuberculosis occasionally produced a severe local reaction in susceptible children. When an ointment one-twentieth the strength of the original preparation was used, no severe reactions occurred, but there were many false negative reactions. For this reason the full strength ointment is now used in patients who have a negative reaction when tested with the diluted ointment.

BRAHDY, Mount Vernon, N. Y.

EFFECT OF PHENYLETHYLHYDANTOIN ON THE THYMUS GLAND. K. KONISHI, J. Pediat. (Tokyo), Oct. 20, 1931, no. 377, p. 1444.

The author fed phenylethylhydantoin to rabbits of different ages in amounts of from 0.07 to 0.09 Gm. per kilogram of body weight, gradually increasing the dose. The total amount of the drug thus given varied from the minimum of 0.1 Gm. in a young rabbit weighing 550 Gm., given in divided doses over a period of two days, to the maximum of 9.3 Gm. in a rabbit weighing 2,200 Gm. fed over a period of twenty-five days. The thymus gland was studied microscopically as was that of the normal, control animal. The author found that phenylethylhydantoin produced an atrophy of the gland, which was directly proportional to the length of time that the drug was administered. The changes in other organs consisted chiefly of hyperemia which, in extreme form, might be recognized as a distinct hemorrhage.

KATO, Chicago.

CHANGES IN THE BONES AS SEEN ON X-RAY FILMS IN CASES OF LEAD POISONING. A. KOGA, J. Pediat. (Tokyo), Nov. 20, 1931, no. 378, p. 1571.

The observations recorded are based on four cases of lead encephalomeningitis in infants whose mothers were habitual users of lead-containing cosmetics. The roentgenograms of the long bones showed definite changes at the epiphyses which somewhat resembled those seen in rickets, congenital syphilis or scurvy, but the picture was decidedly different. The author does not state definitely whether or not these changes are due to lead, but he thinks it probable. The conditions that govern the process of ossification in the growing bones depend on the metabolism of inorganic phosphorus, calcium and carbon dioxide of the blood. In lead poisoning, lead is thought to exist in the body in the form of a phosphate, This causes certain changes in the distribution of phosphorus in the blood. Again, acidosis, which is a rather constant phenomenon in lead poisoning, induces hypophosphatemia. The circulatory disturbance due to the occurrence of endarteritis obliterans at the epiphyses may also alter the process of ossification.

KATO, Chicago.

Society Transactions

PHILADELPHIA PEDIATRIC SOCIETY

Feb. 9, 1932

JOHN P. SCOTT, M.D., *President, in the Chair*

CONGENITAL ABSENCE OF THE GALLBLADDER AND EXTRAHEPATIC DUCTS. Presented by DR. J. MONTGOMERY DEAVER.

The child in the case reported lived for one year and twelve days. In 1908, in a review of sixty-two cases of congenital obliteration of the bile ducts, Lavenson reported only three cases in which the patients lived longer than eight months; two of them lived until the age of 9 months and one until the age of 11 months. In 1918, Ladd reported twenty cases of congenital atresia with stenosis of the bile ducts. Eleven of these patients were subjected to operation; in eight of the cases the condition was amenable to surgical treatment. Six of the eight patients recovered. In 1931, Warren Cole reported four cases in which there was complete absence of all extrahepatic ducts. One of these patients was operated on at the age of 7 months and was alive at 8 months; the other three lived only a few months.

J. R., a white girl, aged 8 months, was admitted to the Children's Hospital of the Mary J. Drexel Home on June 14, 1931, with the chief complaint of yellowness of the skin. No abnormality was noted until the child was 6 weeks old, when it was observed that the sclerae were slightly jaundiced. The jaundice persisted, varying in degree from day to day. The stools were clay-colored, and the urine dark. The family history was irrelevant. The patient was the first child; it was delivered at full term and no instruments used. The weight at birth was 6½ pounds (2,954 Gm.). For two months prior to admission to the hospital there had been a discharge from the ears. The patient was breast fed for the first two months, then dilutions of cow's milk were given. The child did not gain or develop physically. She took her feedings well, and there was no vomiting or tendency toward constipation. Mental development was normal.

Physical examination showed a malnourished, deeply jaundiced, underdeveloped, child 8 months of age, weighing 10 pounds (4,500 Gm.). The edge of the liver was palpable 5 cm., and the spleen 2 cm., below the costal margin. There were definite pea-sized axillary and inguinal glands. Repeated examinations of the stools did not reveal any bile, but urinalyses showed bile. There was moderate secondary anemia, with a normal white cell count. The icterus index was 60; the fragility test was normal. The blood platelets numbered 136,000. The Wassermann and Kahn reactions of the blood were negative.

The course was afebrile. A diagnosis of congenital atresia of the bile ducts was made, and an exploratory laparotomy was performed under ether anesthesia. When the abdomen was opened, the liver was found to be markedly enlarged and showed advanced biliary cirrhosis. The spleen was firm and large. Exhaustive exploration failed to reveal the gallbladder or extrahepatic ducts. The foramen of Winslow was patulous. The abdomen was closed without drainage. There was little postoperative reaction, and the wound healed by first intention. Two months after operation, the child's condition remained the same, and the parents were allowed to take her home.

The patient was readmitted to the hospital two months later with a severe cold in the head. The weight was 9½ pounds (4,125 Gm.).. Urinalysis showed

many pus cells. The stools were very loose, coffee-ground color and positive for blood. The child had a septic temperature, and died on Oct. 27, 1931. At autopsy, the liver was freed and removed en masse with the duodenum, pancreas and stomach. The gallbladder was absent. Careful dissection failed to reveal evidence of extrahepatic ducts. Both macroscopically and microscopically, the liver showed marked biliary cirrhosis with proliferation of the intrahepatic ducts. The duodenum was normal in size and contour. The papilla of Vater was absent, and only a small opening was present for the pancreatic duct. The stomach showed no abnormalities. The kidneys showed multiple hematogenous abscesses in the cortex and parenchyma. The spleen showed passive congestion, pulp fibrosis and hemosiderin pigmentation. The remaining organs, including the pancreas, were essentially normal.

In this case an exploratory laparotomy was performed because the preoperative diagnosis was congenital abnormality of the biliary ducts or atresia of the papilla. Since these conditions are at times amenable to surgical intervention, it follows that such patients should be given the benefit of an exploratory operation. A definite differential diagnosis cannot be made between complete or partial absence or simple atresia of the biliary ducts. Differential diagnoses should be made between icterus neonatorum, cysts and tumors of the head of the pancreas, hemangiomatous malformations of the liver, etc. Since it is well known that cirrhosis follows obstruction to the biliary ducts and that chronic jaundice leads to osteoporosis and intestinal upsets and predisposes to infections, exploratory laparotomy should not be delayed too long.

DISCUSSION

DR. JULIAN M. LYON: Previous to this patient's admission to the Children's Hospital of the Mary J. Drexel Home, she was admitted to the Children's Hospital of Philadelphia. At that time the complaint was jaundice and bilateral otitis media. The white cell count was 26,000, which fell after the ears improved. There was an icterus index of 65 and the van den Bergh test showed 8.1 units. Because of the intense jaundice, the high icterus index, the results of the van den Bergh test, the bilateral otitis media and the general condition, it was considered unwise at that time to perform a laparotomy. A favorable prognosis was not given to the parents, so they removed the child.

It is interesting to note that this child lived for one year and twelve days without a gallbladder or bile ducts. In the absence of bile in the intestinal tract, a great deal of fat is usually lost in the stool, and there is failure to absorb a normal amount of calcium. Apparently, there was no abnormality of coagulation. In jaundice, lack of proper coagulation is at least partly due to the lack of calcium and is often improved by intravenous therapy with calcium, but this child did not need such therapy.

Whipple claims that in embryos of about 3 mm. there is a longitudinal tube-like evagination in the intestines, just caudal to the stomach. The anterior portion of this is rather firm, and the posterior portion is soft. The former portion is known as the pars hepatica and the latter as the pars cystica. By the time the embryo is 12 mm. long this evagination has been pinched off from the anterior and posterior end, so that the only connection that remains with the intestines is the connection with the posterior part which is later destined to be the gallbladder. That connection is the anlage of the common duct, and from it extends a cord of cells, the anlage of the hepatic duct that connects the pars hepatica, the more solid part, which is destined to become the liver. The pars cystica at the distal end of the common duct enlarges and becomes the gallbladder. This differentiation is recognizable by the time the embryo is 12 mm. in length. Anomalies of these parts apparently occur early in embryonic life. Schachner has reported a number of anomalies in the gallbladder and bile ducts. Absence of only the gallbladder is not uncommon, and causes no symptoms, but the absence of the bile ducts—absence of bile flowing into the intestinal tract—has not been

consistent with life. Nevertheless, it is interesting that the child in this case lived so long without either bile ducts or gallbladder, and that the nutrition remained as good as it did, without abnormal coagulation of blood.

SERUM SENSITIVENESS AFTER THE ADMINISTRATION OF TOXIN-ANTITOXIN; A CLINICAL AND LABORATORY STUDY. Presented by DR. LOUIS TUFT.

From a review of the literature and personal experience, it seemed that it was still doubtful whether injections of toxin-antitoxin (equine) induced a sensitivity to horse serum. In order to determine this more definitely, I carried out a series of studies, including tests of the skin, tests of the eyes and examinations of serum for antibodies, both in a control group of one hundred patients who had not received toxin-antitoxin or other serums and in a larger group of patients who had. In addition, questionnaires were sent out to practitioners, inquiring as to the frequency and character of reactions occurring when the injection of serum was repeated. The results of these studies proved rather definitely that after the injection of toxin-antitoxin (equine) into children, 27.9 per cent were sensitized in varying degrees to horse serum; that this sensitization was not limited to the skin, but affected other tissues of the body and finally, that sensitization is more apt to occur in allergic children or children of allergic families.

Reinjection of serums containing larger amounts of horse serum is in certain instances fraught with the danger of severe, immediate or accelerated reaction, and in most instances this may be prevented by the performance of a properly carried out test of the skin (the intradermal injection of 0.02 cc. of horse serum in a dilution of 1:100), in preference to the test of the eye, just prior to administration and in the presence of a positive reaction, either by the use of a nonhorse serum-containing serum or, if this cannot be procured, by the spaced administration of increasing amounts of serum together with the administration of small amounts of epinephrine. In the future, the continued use of diphtheria toxoid or of toxin-antitoxin prepared with goat serum antitoxin in active immunization against diphtheria will prevent the possible development of sensitization to horse serum in immunized persons and obviate the necessity for further precautions with injections of serum.

DISCUSSION

DR. THEODORE MELNICK: In Dr. Wolbert's report of eight deaths resulting from serum sensitivity, five of the patients had previously received toxin-antitoxin, two in previous serum, and one was a victim of horse asthma. This illustrates the importance of being on the alert for sensitivity. At the Philadelphia Contagious Hospital, especially in the scarlet fever department, every child is tested for sensitivity to serum before its administration. In the diphtheria department we are resorting to the cutaneous test for sensitivity to serum, especially in those who have previously received serum or toxin-antitoxin. In the presence of a positive reaction to the skin test, the serum is given in minute doses that are divided and accompanied by the use of epinephrine.

I have had the experience of giving serum to a physician's child who had laryngeal diphtheria and who was subject to hay fever. He had been given toxin-antitoxin but had not received the final Schick test. A positive response to the skin test did not occur. In order to be safe I gave him antitoxin in divided doses, small doses, over a period of eight hours. Twenty-four hours later, a severe serum reaction occurred. With repeated doses of epinephrine the condition was controlled. It is worth while and necessary to make preliminary skin tests for sensitivity to serum.

Dr. Tuft mentioned a certain number of positive reactions to the eye test; did the same persons give a positive reaction to the skin test? Does he know the amount of serum in any of the stock serobacterin preparations?

DR. LOUIS TUFT: Those with positive eye tests also gave positive reactions to the skin tests. None of the patients who gave negative reactions to the skin tests ever gave positive reactions to the eye tests. Some had positive skin tests and

negative eye tests. Never in my experience or in the experience of the men with whom I have talked was there a positive eye test with a negative skin test. The skin test is much more sensitive. There is not enough horse serum in any of the vaccines to make it worth investigating.

THE EFFECT OF DEHYDRATION ON THE ALLERGIC RESPONSE. Presented by DR MITCHELL I. RUBIN.

A brief review of recent advances in the treatment of asthma in children by the means of rendering the body tissues acid in reaction was presented. The benefits resulting from this form of therapy, the author believed to be due probably to the dehydration induced by the acidosis. Other evidences showing that dehydration alters allergic responses both in clinical disease and in experimental conditions were cited.

Dr. Kellet and Dr. Rubin made a study of the effect of dehydration on anaphylaxis in guinea-pigs passively sensitized to horse serum. The results were that 75 per cent of the animals dehydrated by water starvation (dry foods) were saved from anaphylactic death; whereas 100 per cent of the control animals died from this shock. It was further shown that dehydration also protected guinea-pigs from shock when histamine was given intravenously.

A discussion of the manner in which dehydration affects the mechanism of anaphylaxis was presented. The experiments seem to point to the fact that an alteration of the neurovisceral unit has occurred. This results in a modification of the response when antigen is injected into the passively sensitized animal. Studies of the blood made on these animals showed that acidosis was not present during the state of dehydration. Interesting changes in the albumin-globulin ratio of the blood serum were noted and discussed. Experiments carried out on the uteri of passively sensitized animals showed that alteration in the anaphylactic contractions can be produced by changes in the magnesium content of the bathing fluid, when a modified Dale apparatus is used. Increased amounts of magnesium in the fluid resulted in a decrease in the amount of contraction of the uterus.

A few interesting clinical observations on the effect of dehydration on asthma and eczema were mentioned.

DISCUSSION

DR. RALPH H. SPANGLER: Dr. Rubin's findings point to a possible valuable, clinical application. As 1 Gm. of carbohydrate holds 3 Gm. of water in the tissues and 1 Gm. of fat holds only 0.1 Gm. of water in the system, I have been using a diet with a high fat and low carbohydrate content—not a strictly ketogenic diet—in the treatment of patients with a family history of allergy who exhibit such clinical evidence of allergy as asthma, hay fever, urticaria and similar symptoms. Cannavo reports that all acids of the aliphatic series produce acidosis, but that only those that have an odd number of carbon atoms are intensely ketogenic. Olive oil and cod liver oil fulfil this requisite. Fleuret reports that the addition of hydrochloric acid to the food diminishes the excretion of ketone bodies. The production of a ketosis therefore is probably largely effective in lessening sensitivity by inducing dehydration. Magnesium sulphate, U. S. P., is valuable as a dehydrating agent.

Clinically, it would seem that many of us have been inadvertently lessening sensitivity by inducing dehydration through various means which tend to reduce the intracellular and extracellular water content of the body. Therefore, Dr. Rubin's investigation throws considerable light on the mechanism of some of our empiric therapeutic measures. Irvine McQuarrie recently reported on the use of pitressin, an antidiuretic extract of the posterior lobe of the pituitary gland, and he has been able to produce convulsions in potentially epileptic children by increasing the state of hydration. His findings seem to lend support to the probability that epilepsy may be related to allergy. From a clinical standpoint, Dr. Rubin's findings offer possibilities which to me are fascinating.

CHICAGO PEDIATRIC SOCIETY

BERT I. BEVERLY, *Secretary*

Regular Meeting, Feb. 16, 1932

H. E. IRISH, M.D., *President, Presiding*

PROPHYLAXIS OF ANEMIA OF PREMATURE INFANTS. A PRELIMINARY STUDY CONCERNING USE OF VARIOUS AGENTS IN THE PREVENTION OF DEVELOPMENT OF SO-CALLED PHYSIOLOGIC ANEMIA OF PREMATURE INFANTS. DR. ARTHUR F. ABT and DR. BETH REYNOLDS NAGEL.

The experimental work reported was carried on in a special ward for premature infants, under ideal conditions. After the infants were discharged from the hospital they were followed in the outpatient department, returning at intervals to a special premature clinic.

All infants selected were healthy premature infants, i. e., there was no history or sign of syphilis, hemorrhage, infection or other disorders that might be taken as a cause for anemia. In our work we divided them into two distinct classes; those born after from six to seven months' gestation and those born after eight months' gestation. This was necessary because it has been shown that the more premature the infant and the less the birth weight, the more severe the anemia. This differentiation was likewise made with the control series.

In the prophylaxis of premature anemia it may be concluded that treatment with iron preparations alone is of doubtful value. Further, neither the use of desiccated pig's stomach (ventriculin) nor the use of liver fraction alone proved of value in the prevention of anemia.

Favorable results seem to have been obtained in the prophylaxis of the anemia of premature infants through the use of a dried liver fraction combined with ferrous ammonium citrate.

The most marked results in this series of experiments were obtained in the group of premature infants of from six to seven months' gestation, in whom the development of the anemia was most severe. No definite conclusions as to the etiologic factors causing this anemia can be formulated from the experimental data which we obtained. In a review of the literature, the following theories of the cause of anemia of premature infants are most tenable: (*a*) the lack of an adequate iron reserve depot, and its early depletion, and (*b*) a functional insufficiency of an imperfectly developed hemopoietic system.

The chief objection to the depleted iron reserve depot as an explanation of physiologic anemia of prematurity is the fact that the prophylactic feeding of iron has not prevented the development of anemia. Possibly the iron, even though administered in large doses, has been resorbed and retained only in minute quantities.

The functional incapacity of the hematopoietic system may be analogous to the incomplete and imperfect development of the gastro-intestinal, cardiovascular and heat regulating systems of the premature infant. At the sixth or eighth month of intra-uterine life, the hematopoietic system is probably still somewhat imperfectly developed, and therefore functionally incapable of adequately responding to the additional demands of extra-uterine life.

This theory would help to explain the lower erythrocyte and hemoglobin values found in the premature infants of from six to seven months' gestation as compared to the premature infants of eight months' gestation. The exact mechanism of the development of this anemia remains unexplained.

THE RUBBER TUBED PIPET IN THE FEEDING OF SMALL PREMATURELY BORN INFANTS. DR. L. W. SAUER.

Many prematurely born infants weighing 2, 3 and 4 pounds (0.9, 1.4 and 1.8 Kg.) will grow into normal children if sterile breast milk can be introduced into the

stomach in sufficient amount at regular intervals. Gastric juice is already present: digestion, assimilation, gain in weight and growth occur at a gratifying rate if anomalies and birth injury are absent. Intelligent nursing care is a prerequisite; i. e., infection and chilling must be prevented. Because such infants are too immature to suck and swallow sufficient food, gavage has become the universal method of choice. Although some of them can suck and swallow, the energy so expended delays gain in weight and growth.

In a forthcoming number of the AMERICAN JOURNAL OF DISEASES OF CHILDREN will be described a method in use for more than six years in the early feeding of eighteen premature infants weighing less than 4 pounds (1800 Gm.). No infant weighing more than 2 pounds (900 Gm.) has died when the rubber tubed pipet was used. Nurses find the technic simpler, less time-consuming and safer than gavage. In no instance has milk or water been aspirated, nor has

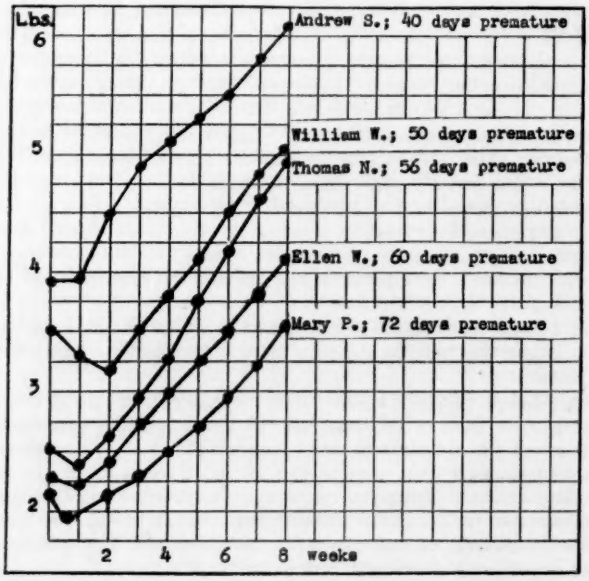

Chart showing weight of five prematurely born infants with birth weights of less than 4 pounds.

cyanosis been attributed to the technic. The accompanying chart shows how readily such small infants gain weight if free from congenital defects and trauma. The initial loss in weight seldom exceeds a few ounces. It will be seen that after the first week the rate of gain usually compares favorably with the intrauterine rate. The technic is usually as follows: Within a few hours after birth from 1 to 2 fluidrachms of warm, sterile water is introduced by drops into the pharynx from the rubber tubed pipet (Glasco, no. 2150, 6 inch pipet with extra large bulb). Within four hours after birth an equal amount of sterilized breast milk is given seven or eight times in twenty-four hours. This is soon increased to 3 and then to 4 fluidrachms and more. Only boiled breast milk is fed. Fluoroscopic and roentgenographic observations with sterilized barium breast milk in a thriving 4 pound infant show clearly that milk introduced into the pharynx flows down the esophagus into the stomach. After the infant has gained sufficient strength and weight, the same outfit serves as a diminutive Breck feeder until the child can take a small Breck nipple or nurse at the breast.

Observations on a nonviable, about ninety days premature, fetus weighing about 1½ pounds (700 Gm.) showed that during the first few hours after birth sucking and swallowing reflexes can be elicited; i. e., the nervous center is sufficiently developed to function, but the muscles are too feeble to complete the acts of sucking and swallowing. The infant would suck on the tube placed between the lips, but could not draw milk. After a few futile attempts, the child would go into a deep sleep. After a few hours the breast milk was given into the pharynx as above outlined. The milk disappeared without being swallowed. Post-mortem examination about twelve hours after birth showed breast milk in the stomach and upper part of the intestine; the lungs had expanded fairly well; no milk had been aspirated.

I believe that the method warrants a trial.

DISCUSSION

DR. GERARD N. KROST: How rapidly does Dr. Sauer introduce these feedings? Is it done more quickly than with the medicine dropper on the tongue, and can the plan be used for older infants if necessary?

DR. LOUIS W. SAUER: The time consumed in the giving of a feeding varies with different babies, but it usually takes less time than for a gavage feeding. My associates and I spend probably ten minutes in giving an ounce of food. As the infant gets a little older this outfit works very well as a diminutive Breck feeder. When the baby can suck and swallow, he can feed himself. Otherwise, by pressing gently on the bulb, the milk runs down the esophagus into the stomach.

DR. HENRY D. CHAPIN (New York): As the members of this society know, in the East, and I suppose here, there has been a great reduction in mortality due to the work of pediatricians. Twenty years ago infant mortality ranged between 80 and 90 per cent. During 1931 it was 56 per cent, but there has been practically no reduction in the mortality during the first month of life. It was a question of how one could reduce that early mortality as it had been reduced in the older infants. If it was due to congenital defects, nothing could be done, but it seemed to me that if all the breast milk desired could be obtained, it would be of great assistance. I had in mind the Federation in New York, and my associates and I made an effort to secure breast milk for premature babies. We started with one room, which was given to us by the health department, for the collecting of milk. We now distribute 5 or 6 quarts of breast milk a day, which can be procured for premature babies and sometimes for poorly nourished babies. We pay the women fifteen cents an ounce for the milk and insist on securing the milk at our stations. We started to send nurses to the houses, but found on several occasions that the milk had already been collected and that some of the women were watering their milk. We now have two stations, one in Brooklyn and one in New York. The greatest care is exercised. We do a Wassermann test and an examination of sputum on every woman, and the milk is collected with aseptic care.

We have handled just less than 4,000 premature infants since the work was started and have saved 70 per cent of them. We have distributed over 23,000 quarts of mothers' milk. We have no difficulty in collecting it, and these women are very grateful to us. We feel that we have served a good social purpose here. These women would have to go out and work, but if they can stay at home and sell their extra milk that is an advantage. To one woman we paid $936.00, and during that time her own children were watched carefully and kept in good condition. Another woman has collected over $1,100.00 from us. We have in this plan something that will help these women so that they can remain at home and nurse their own babies.

We also find that even a few weeks' care, carrying these babies over the critical time, will often be sufficient to save life. We feel that this is a valuable social effort, not only in saving infant life but in helping needy persons.

PNEUMOTHORAX IN CHILDREN. DR. EUGENE T. MCENERY.

Pneumothorax in children will be discussed as it occurs in the progress of a case of pneumonia, with its most frequent complication, empyema. These conditions have occurred in a series of 131 cases of empyema, following pneumonia, during the years from 1928 to 1931, inclusive, at the Childrens' Memorial Hospital.

To classify these pneumothoraxes, I have divided them into three types: 1. Spontaneous pneumothorax, which occurs before any treatment of the empyema had been instituted. 2. Traumatic pneumothorax, which follows aspiration of the pleural cavity in the removal of fluid. 3. Small localized pneumothorax, which is seen occasionally with or without empyema.

In our series of 22 spontaneous pneumothoraxes, all were due to empyema, following pneumonia. The organisms responsible for the empyema pneumococci, except in 4 cases (3 which were due to pyocyaneus, hemolytic streptococci and Staphylococcus aureus and 1 in which no culture was made). Three of the twenty-two patients were cured without treatment except the spontaneous coughing up of pus. In two cases surgical drainage was done, and in the others aspiration was employed. Six deaths resulted, a mortality of 27 per cent.

The second group of cases is of interest on account of the method of production of the pneumothorax. In the method that my associates and I use in the aspiration of chests, we do not inject any air, but try to prevent any from entering the pleural cavity. These pneumothoraxes were produced, then, not by air getting in from the outside but by air escaping from the lung itself. The third type includes the small localized pneumothoraxes that may be seen in the course of pneumonia, with or without empyema. At first they appear on the roentgenogram as an increased area of density; this may persist for several days, and then a slight clearing appears in the center, which gradually enlarges and assumes a more definite, clearcut outline which may remain for a day or for months and then disappear almost as quickly as it appeared.

In conclusion I have presented a series of 81 cases of pneumothorax following pneumonia with empyema, in a series of 131 consecutive cases of empyema. Of these, 22 pneumothoraxes were spontaneous, 59 were traumatic and 4 were localized. There were 71 recoveries with 14 deaths, a mortality of 16 per cent. Pneumothorax in children, I feel, does not seriously complicate a case of empyema, except in a check-valve type, and its occurrence aids in the following of the fluid level in the roentgenograms.

AN ATTEMPT TO USE THE SPINAL FLUID AS A BIOLOGIC TEST IN THE DIAGNOSIS OF TUBERCULOUS MENINGITIS. DR. BENJAMIN GASUL and DR. PHILIP ROSENBLUM.

The theoretical considerations for the use of the patient's spinal fluid, which has been properly evaporated and dialyzed, as an intracutaneous biologic test in the diagnosis of tuberculous meningitis are presented.

No positive reaction to tuberculin was obtained when 0.2 cc. of spinal fluid from 116 patients with conditions other than tuberculous meningitis was injected intracutaneously. When injected intracutaneously into 7 patients with tuberculous meningitis, 0.2 cc. of spinal fluid, which had been previously evaporated and dialyzed, gave only 2 positive reactions to tuberculin. When the same spinal fluid was injected intracutaneously into healthy, but tuberculously infected, children, 5 gave a positive reaction to tuberculin.

While we believe that patients with conditions other than tuberculous meningitis will not give positive intracutaneous reactions to tuberculin with their own spinal fluid, the number of tests performed on patients with tuberculous meningitis is too small for any definite conclusions to be drawn.

BERT I. BEVERLY, *Secretary*

Clinical Meeting, March 15, 1932

MAURICE L. BLATT, M.D., *in the Chair*

INFANTS' AND CHILDREN'S DIET. DR. SAMUEL NICHAMIN.

In the effort to assist the infant in coping with its surroundings, close adherence to the optimum in nutritional principles is particularly stressed. Many factors, practical as well as theoretical, must be considered in the choice of an infant food in an institution in which there is a large number of children to feed. Simplicity in the formulas is an important requisite. Because of the small amount of help and the large numbers of bottles to be made, the formula should be of a type that is easily prepared, manipulated and changed. The handling and transferring of the bottles from the diet kitchen by irresponsible and numerous attendants on the various floors necessitate a milk product that possesses at least relative sterility. The inability of the infant to finish its prescribed feedings unaided results in a diminished total of the amount taken. The necessity for the use of concentrated formulas, so that the caloric intake may remain adequate with the smallest volume, is then apparent. In addition, a rather concentrated form of food is necessarily required for premature and dystrophic infants. Finally, together with a high caloric value the food should be easily digestible and assimilable.

Mead's powdered lactic acid milk no. 2, plain, most nearly covers all these requirements, and has proved to be more successful clinically than other milk products at St. Vincent's Orphanage. Whole boiled milk, raw milk and powdered whole milk have been used in individual cases, but not in a routine manner. Powdered protein milk with its low carbohydrate and high protein content is used in cases of dyspepsia and severe marasmus. The basic formula used in this institution includes these milk products, prescribed so that they represent from 1½ (45 cc.) to 2 ounces (59 cc.) of milk per pound of body weight for twenty-four hours; 3 ounces (89 cc.) of fluid per pound for twenty-four hours, and ⅒ ounce (3 Gm.) of carbohydrate per pound for twenty-four hours. The carbohydrate primarily used is Mead's dextrimaltose and occasionally Karo syrup, in amounts not exceeding 1½ ounces. Cereal is given at 4 months, and pureed vegetables at 5 months. Finely divided stewed fruits are given once daily, together with custards, jello, etc. Water is given to all infants three times daily, and serves as a vehicle for medications whenever indicated. Cod liver oil and orange juice are given in the first month in amounts of 0.5 drachm daily, which are gradually increased to 3 drachms of cod liver oil and ½ ounce of orange juice daily, included in the 10 and 6 o'clock bottles. Treatments with quartz light are given to the babies twice weekly. At 8 months the babies are transferred to the floor for the older children, and the formulas are changed gradually to whole milk. For the older children, the diet consists of three principal meals, with milk offered in the afternoon and before bedtime. The meals include cereal, toast, bacon, eggs, vegetables, jello, pudding, etc. At all meals, liberal portions are served, so that the child is guided entirely by its own appetite as to the amount taken. Interestingly, there is no problem of anorexia in the institution. The gains in weight of these children are progressive, and in growth and development they closely approach the normal for their respective ages.

FIXATION NYSTAGMUS. DR. SAMUEL J. HOFFMAN.

Baby W. A., aged 6 months, was a "door step" baby brought in by the police, and therefore no history was available.

Examination revealed a well nourished white boy, with the fontanel closed.

General examination revealed occasional shaking of the head; there was a constant fixation nystagmus. By this is meant that there was an interference

with central fixation on the basis of a pathologic process in the optic pathway. It was a spontaneous horizontal nystagmus of the rhythmic pendular type. When the attention of the child was attracted and the child looked to the right, there was a quick component to the right; when he looked to the left, there was a quick component to the left; when the child was left alone, the slow rhythmic pendular spontaneous nystagmus recurred. There was a right convergent squint, not due to paralysis of a muscle, since there was full excursion laterally and medially.

Vision was present, since he followed the light with his eyes. The eyegrounds showed moderate pallor of both disks. The disks were sharply outlined. Apparently, the condition was not the atrophy that follows a choked disk or papillitis. The rest of the examination gave essentially negative results. No pathologic reflexes were present.

Examination of the spinal fluid showed 1 cell, 45 mg. of sugar and normal pressure. The Pandy test gave negative results. Encephalography was done by Dr. Levinson; 62.5 cc. of spinal fluid was removed and replaced by 60 cc. of air. The spinal fluid was under normal pressure, and 2 cells were found.

Thus this is a case of fixation nystagmus, which I believe is due to a cerebral injury, probably a diffuse hemorrhage involving the base of the brain and cortex, causing cortical atrophy as well as optic atrophy. The microcephaly that is present undoubtedly aggravates the condition.

SPINA BIFIDA. DR. FRANK V. THEIS.

Mary Ann was born in the house on Dec. 14, 1929. Her weight at birth was 7 pounds (3,175 Gm.), and this fell to 6 pounds (2,727 Gm.). An orange-sized cystic swelling located in the lumbosacral region was diagnosed as a meningocele. The patient was transferred to St. Joseph's Hospital on Feb. 18, 1930, and prepared for operation. Because of the poor general condition of the infant, surgical intervention was postponed until April 24. Preoperative examination for hydrocephalus and paralysis gave negative results. The weight increased to 10 pounds (4,535 Gm.). The condition of the cyst and surrounding skin was satisfactory. A myelomeningocele was found at operation. Excision of the sac and plastic closure of the soft tissues over the defect in the vertebral column were performed under local anesthesia. Uneventful convalescence and primary healing of the wound followed.

At 6 months, the infant weighed 11 pounds (4,988 Gm.); at 18 months, 21 pounds (9,500 Gm.), and at 2 years, 23 pounds (10,400 Gm.). Now the child is normal in every respect. She has walked since the age of 16 months, and the knee and plantar reflexes are normal.

A previous case was instructive along this line and influenced the delay in operation on Mary Ann. A child was referred to me four days after birth with a ruptured lumbosacral spina bifida. The infant was apparently in good health, but no precautions had been taken to protect the lesion from contamination by the diaper. Following careful preparation of the field for operation, the remaining portion of the sac was removed. The operative findings of a meningomyelocele were similar in both children. Uneventful convalescence with primary healing of the wound followed. The infant was discharged from the hospital on the tenth day after operation. Repeated examinations failed to reveal evidence of hydrocephalus until the end of the second month. Progressive hydrocephalus followed. Death occurred four months later. Immediate operation was indicated by the danger of meningeal infection. The possibility of hydrocephalus was decided to be the more remote of the two dangers.

With a closed spina bifida sac there is no necessity for haste in operating. Delay is warranted in order to improve the physical condition of the infant to

lessen the danger. The important function of the meningeal lining of the sac is preserved until stabilization of secretion and absorption of the spinal fluid occur. Amputation of the spina bifida sac with plastic closure gives excellent results in selected cases.

ANEMIA. DR. JOSEPH GREENGARD.

During the past two years, Dr. Maurer and I have been interested in the study of anemia in some infants we have kept under observation. We have used several types of therapy in different groups. In one group we used inorganic iron; in another, liver extract alone, and in a third group, a combination of liver and iron.

During the course of this study we were impressed by the fact that there seemed to be a distinct change in general nutrition in the patients receiving liver extract and the combination of liver extract and iron.

In general, it may be said, the results we have to show are not in the nature of an absolutely controlled experiment. In the first place, according to our observation, the children in this institution are divided into two definite groups. First, there is a group of children in whom the blood picture is quite good and who progress rather well nutritionally and gain weight without any particular type of therapy. In the second group, there is rather severe anemia, and, in addition, the children are nutritionally rather poor specimens. The first group receives no treatment, but one cannot consider it an adequate control group.

I wish to show you a few records of children, some of whom have received no treatment, some only iron, some liver extract and some a combination of liver extract and iron. We shall show you the charts and you can draw your own conclusions. We have not picked the best charts, but have selected those that seemed most representative.

In general, a distinct upward turn in the curve for weight has been noted shortly after the introduction of the liver extract, without an accompanying marked increase in caloric intake. A similar apparent stimulus to growth has been noted following the introduction of vegetables in the dietary.

THE EFFECT OF LIVER EXTRACT AND IRON ON THE BLOOD PICTURE. DR. SIEGFRIED MAURER.

This work has been carried on for about one year. The series is now small and only statistically suggestive. Owing to the constant removal and addition of the infants in the wards each year, only a small group has been subjected to a prolonged, continuous study.

The patients were divided into two groups: one comprising infants who were making satisfactory gains in weight and who appeared to progress normally in development, and the other, a treated group, composed of infants who were gaining weight slowly, who were distinctly below the average weight for their age and whose blood counts demonstrated anemia.

In the untreated group an average of 18.9 Gm. of hemoglobin at birth and 13.9, 11.1, 10.2, 10.2, 10.2, 9.9 and 10.6 Gm., respectively, from the ages of 1 to 7 months, inclusive, was noted. These values are approximately the same as those found in McKay's series of unselected cases in which treatment with iron was given.

The second, or treated group, showed 15.5, 10.7 and 9.2 Gm. of hemoglobin, respectively, at the ages of 1, 2 and 3 months. Liver extract and iron were given at this age, and the hemoglobin rose gradually to 9.3, 9.8, 10.6 and 10.7 Gm. at the ages of from 4 to 7 months, inclusive. That is, after three months of treatment, the hemoglobin had reached the value of that in the untreated group.

THE PROPHYLAXIS OF DIAPER ERUPTIONS. DR. MAURICE SCHNEIDER.

Eruptions of the buttocks described by Parrot in 1877 as lenticular syphilis were found to be late stages of Jacquet's dermatitis in 1886. Jacquet, in 1900, described the lesions as simple erythema, erythematopapular, erythematovesicular and erosive forms. Adamson, in 1912, first ascribed the etiology of these erup-

tions to a local irritation from the urine and feces. He also found diaper dermatitis more frequently in babies with vasomotor instability, eczema and lichen urticatus. In 1922, Crawford suggested the use of boric acid, phenol and cresol in the last rinsing water of diapers. In 1926, Cooke described Bacillus ammoniagenes, capable of converting urea and of liberating ammonia, as the etiologic factor in diaper eruptions.

In an institution like St. Vincent's Orphanage diaper dermatitis is a constant problem. Diapers are changed on a schedule of from two to four hours; apparently a sufficient time is allowed for ammoniacal decomposition. Following the orders of Dr. Blatt, 1 pound (500 Gm.) of boric acid was added to the last rinsing water (37 gallons [1,401,449 cc.] in the diaper laundry, and irritation of the buttocks subsided.

In an epidemic of diarrhea, in 1930, severe irritation of the buttock was noticed. This irritation spread outward from the anus, in contradistinction to true Jacquet's dermatitis, which was also present at that time. In some cases, ulcerating forms were present. Following the subsidence of the diarrhea, irritation due to the diarrhea ceased, but the other lesions persisted.

Active treatment of Jacquet's dermatitis consisted of sponging with boric acid, application of aluminum acetate and of hydrosol ointment, exposure to air and sunlight and the use of ultraviolet rays. All lesions responded to this form of treatment.

Since the use of 1 pound of boric acid to about 37 gallons of water produced good results in preventing dermatitis, Dr. Blatt sought to find out the amount of boric acid in the dry diaper. Analysis of the solution formed by dissolving the contents of a dry diaper in 1,000 cc. of distilled water showed an average of 0.12 Gm. of boric acid in the dry diaper. An analysis of the last rinsing water showed an average of 0.2 Gm. of boric acid per hundred cubic centimeters.

When 0.1, 0.06, 0.04 and 0.03 Gm. of boric acid was placed in test tubes into which urine was collected, no ammoniacal decomposition occurred after standing for twenty-four hours.

It is worthy of note that such a small quantity of boric acid as 2 teaspoonfuls per quart seems sufficient to prevent diaper eruption.

DISCUSSION

DR. M. L. BLATT: This work is of interest because of its demonstration of the effectiveness of a small amount of boric acid in each diaper. One pound of boric acid in 37 gallons of water is a small amount. For household purposes, this is the equivalent of 1 tablespoonful to 1 gallon of water. This amount is sufficient to prevent the ammoniacal odor in the wards and to keep the erythema of Jacquet at an exceedingly low incidence.

A STUDY OF THE EFFICIENCY OF MASKS. DR. MAURICE L. BLATT and DR. MAURICE L. DALE.

Gauze masks have been used for many years to prevent the dissemination of mouth spray in hospitals for contagious diseases and in operating rooms. The common gauze mask has been found to be so inefficient that many physicians have dispensed with its use. We tested the efficiency of the commonly used masks and several of our own design and finally found one that we consider satisfactory. Our tests were conducted in a dust-proof tunnel lined with sterile sheets, blood agar plates being used to catch the organisms at distances of 2 inches (5 cm.), 1 foot (30 cm.), 3 feet (91 cm.) and 5 feet (152 cm.). Each mask was tested while new, after four hours' wear and after twelve hours' wear. Between four and twelve tests were made on each type. The ordinary gauze mask, made of six layers of 18 by 22 inch (45.72 by 55.52 cm.) gauze, allowed 25 per cent of organisms to pass through, even when new. A wet mask was no better. A similar mask impregnated with glycerin or with aluminum subacetate reduced the organisms passing through to 15 per cent. A mask made of one layer of small check dimity allowed only 10 per cent of organisms to pass through. Mellinger's wax paper mask reduced the organisms in the 3 and 5

feet plates to about 2 per cent, but permitted the plates at 2 inches to receive 25 per cent of the organisms. Masks used by Weaver and by Capps made of three layers of 44 by 40 mesh (111.76 by 101.6 cm.) gauze gave good results, filtering out all but 10 per cent of the organisms. The same masks impregnated with merthiolate or with hexylresorcinol gave slightly better results, especially after several hours' wear.

Since masks made on the filtration principle were not adequate, Dr. Blatt and I designed a mask on the deflection principle which discharges the exhaled air to the sides. It is made of a sheet of moisture-proof cellophane sewed between two layers of 32 by 30 mesh (78.74 by 73.66 cm.) gauze. A transverse crease across the middle, held in place by a special arrangement of the ties, gives it the tunnel shape that causes the air to pass laterally, away from the patient. The particles of moisture, because of their greater weight and momentum, are not so easily deflected, and thus strike and stick to the gauze on the inner sur-

Comparison of Plain Gauze Mask with the Blatt Mask

	Plain Gauze Mask				Dr. Blatt's Mask			
	No Mask	New Mask	4 Hr. Worn	12 Hr. Worn	No Mask	New Mask	4 Hr. Worn	12 Hr. Worn
2"	40.5	11.5	9.6	39.7	33.2	0.0	0.7	0.3
1'	14.2	4.3	4.9	4.0	7.3	0.3	0.0	1.2
3'	3.4	2.7	2.0	2.7	2.3	0.8	0.5	1.3
5'	2.9	1.9	2.9	4.5	1.7	0.5	0.7	0.7
At sides	...	...	...	...	0.2	0.3	1.0	1.8

face of the cellophane. Thus even the air discharged at the sides is practically sterile. The tests showed that this mask reduced the number of organisms on all of the plates in front of the subject to practically zero, and the plates held at the sides in the path of the discharged air showed only an occasional organism.

Several hundred of these masks have been used, and have been found to be very comfortable.

The accompanying table of bacteriologic data compares the plain gauze mask with the Blatt mask.

URINARY INFECTIONS. DR. RUSSELL D. HERROLD.

A group of adult patients with chronic infections of the genito-urinary tract have been studied by repeated determinations of the hydrogen ion concentration and cultures. A noninfected group has served as a control. The average reaction normally is moderately acid (hydrogen ion determination, 5.7), but in children the average range may be less acid because of a diet high in milk carbohydrates.

Acidifying drugs alone give clinical benefit, as indicated by a decrease in the amount of pus and a subsidence of symptoms with cure apparently as often as with many of the urinary antiseptics. The urine must be kept very acid constantly, since it tends to vary greatly from day to day and from one voiding to another.

The reaction in the absence of residual urine is not influenced by the growth of the colon bacillus within a short period of time, but in the presence of staphylococcus infection the urine in the bladder may become more alkaline if the interval between voidings is more than six or eight hours. Fresh urine may be sterile when inoculated on solid mediums, but subcultures made after the incubation of such urine frequently give large numbers of colon bacilli and staphylococci. Therefore, the criterion of cure must attain a sterile urine after incubation. Chronic infections are common in adults and produce symptoms indicative of damage. Further study is needed of these chronic foci with a view to bacteriologic cure in addition to clinical improvement.

INTRACRANIAL HEMORRHAGE IN THE NEW-BORN FOLLOWING NORMAL LABOR. DR. WADE MARTIN.

The early death of apparently healthy new-born infants following normal labors and deliveries is a keen disappointment to all concerned. The attending physician is frequently confused for want of a good explanation as to why such

a fatal accident should occur following a normal labor and a normal delivery. Pediatricians called in for consultation at this time can only console. Resistant tissues of the birth canal, slight disproportions between the fetal head and the true bony pelvis, prolonged labor because of uterine inertia, prematurity, toxemia of the new-born infant, too rapid labor, breech positions and forceps deliveries have all been given much attention in the literature. Instruction to students and interns with regard to the factors causing intracranial hemorrhages in the new-born are well covered and known by all. However, little appears in standard textbooks about the fact that too much support on the perineum by the physician's hand, in order to save a tear or laceration, may become a factor in causing intracranial hemorrhage. Little is said to medical students on this important bit of technic. Interns are taught how to put pressure on the perineum in order to save it from tears, and they really feel proud and mention the fact that they have delivered so many infants without a tear.

Perhaps many of you have observed the supervising obstetric nurse holding back a soft head with a sterile towel or a sterile pad in order to perfect the sterile routine dress-up. Perhaps the intern delayed delivery by pressure on the perineum against strong pains, waiting the arrival of the attending physician. These hindering procedures happen, but are not recommended. They interrupt a physiologic process, and they are unsafe to the fetal head.

The technic of making a normal delivery of the head seems to vary as regards the amount of pressure applied. When the head appears definitely, bulging the perineum fairly well, some operators, with a sterile towel in their hand, cover not only the perineum but also the rectum and the area posterior to it. With this position they are able to push the head upward and backward with great force against the expelling forces of the uterus and abdominal muscles, and there is also danger of stemming the occiput too forcefully underneath the pubic arch at the same time. The occipital region of the fetal head is probably held too long and too hard under the pubic bone in many instances in an endeavor to save the perineum. Almost all physicians are agreed on the value of episiotomy in shortening the course and relieving the pressure of tissue.

The technic most desired is to steady the perineum aseptically with pressure only enough to aid the occiput to stem underneath the pubic arch, while the head is born by extension.

Comparative Reactivity of the Skin of Mothers, New-Born Infants and Older Infants with Reference to Intradermal Injection of Staphylococcus, Gonococcus and Diphtheria Bacillus Antigens.

Dr. Alfred J. Kobak and Dr. Joseph Greengard.

A preliminary report is herewith presented whereby three groups of mothers, new-born infants and older infants were given intradermal injections of the following preparations: (1) Staphylococcus aureus filtrate, 1:100 of 100,000,000 per cubic centimeter suspensions of vaccine in doses of 0.1 cc.; (2) gonococcus vaccines, the dilution being determined biologically and given in doses of 0.05 cc., and (3) diphtheria toxin given intradermally (Schick test dosage). The antigens were injected into both adults and infants in the same dosage, and pregnant women, puerperal mothers and their babies and infants of varying ages were studied. Under these conditions, about 150 tests were made with staphylococcus filtrates and vaccines. Another 150 tests with the gonococcus vaccines and 518 Schick tests were similarly employed in adults and babies. Our results are similar to those of other investigators using specific and nonspecific antigens, and are comparable with the results found in young animals studied for cutaneous reactivity. While a large percentage of the mothers responded to intradermal injections of the antigens with an erythema reaching from 3 to 4 cm., the greatest majority of their newly born infants gave either no reaction, or an occasional small reaction of about 1 cm. The puerperal patient usually had a larger reaction than the pregnant patient, who in turn was found to exceed the nonpregnant woman in responses of the skin. Thus, in comparing

the reactivity of the skin of a new-born infant with that of its mother, one must bear in mind that one is dealing with extremes of sensitivity, which appears to be greatest in the puerperal mother and least in her infant. The percentage incidence of positive reactions increased when injections were given to the older group of infants.

SMALLPOX VACCINATION. DR. HENRY C. NIBLACK.

Dr. Blatt and I began vaccinating the infants and children of the institution in November, 1931, using the following plan. The children were divided into seven series as follows: three series were given intradermal injections of vaccine of 1 : 4, 1 : 50 and 1 : 100 dilution; the other four series were vaccinated respectively, by the scratch, the multiple pressure (acupuncture), the multiple puncture (prick) and the Pirquet scarifier method.

I was interested in various methods of vaccinating, because the board of health of this city, with which I am associated, had just changed the method of vaccinating school children. For several years it had used the scratch method and felt it was fairly fool-proof. This year it adopted the multiple pressure technic, as recommended by the United States Public Health Service. It has now completed 65,000 vaccinations, and is well pleased with the results. In this series only 15 per cent of the children did not give a reaction; we think this is a very good percentage for a group of men previously untrained in the use of this technic.

The children under discussion were divided into two age groups, those under and those over 1 year. For forty-eight hours before vaccinating a group, rectal temperatures were taken every four hours. Acetone and alcohol were alternated for each child as an antiseptic for preparing the field. The dilutions of vaccine were prepared by the United States Standard Products Company.

I wish first to show a series of vaccinations by the multiple pressure method. (Five babies were presented.) These babies represent a four day, a seven day, a nine day, a two week and a two month interval since the vaccination.

The series shows the typical course of vaccinia, beginning with the vesicle at the end of the first week and ending with a typical scar at two months. The 1 cm. scar is not in the least disfiguring, but fulfils all of the typical requirements.

This next group of babies (seven in number) represents a series vaccinated by the intradermal method with a 1 : 50 dilution of vaccine. Of the 1 : 50 and 1 : 100 dilutions 0.1 cc. was injected, and of the 1 : 4 dilution, 0.05 cc. was used.

In practically all of these babies high temperatures developed on the first or the second day after the injection, and a more or less irregularly intermittent rise in temperature tended to continue for a period of from one to three weeks.

One of the strong arguments for the intradermal method is that a mild vaccinia results in a nondisfiguring scar. That is true in some cases, but a few of these babies had just as typical and as severe a vaccinia as that occurring with other methods, and the usual scars resulted.

These seven babies represent the following intervals: Six days, eight days, two weeks, three weeks, one month, four months and three and three-fourths months. One of these babies represents what might be termed a severe reaction; there will be a typical scar when healing occurs. The argument that this is a good cosmetic procedure is not always true.

Another form of reaction, not a typical vaccinia, as there is no pustule or scab, consists of a hard, erythematous papule, which exfoliates and finally results in a small dimple. This gives a reaction of immunity just as do the typical reactions.

We have not as yet vaccinated a sufficient number of patients to enable us to draw any conclusions; nor are we trying to establish a brief for any method. A further report will be made later.

Book Reviews

The Rheumatic Infection in Childhood. By Leonard Findlay, M.D. Price, $3.50 net. Pp. 180, with illustrations. New York: William Wood & Company, 1932.

In view of the eminence of the author, it is not surprising that this book is well written and carefully thought out. It consists of the various experiences with 701 cases in the Royal Hospital for Sick Children in Glasgow.

The subject is taken up from the practical standpoint and shows a vast amount of work with an unusually complete study. Not only is this true, but the deductions are conservative and useful. American readers will be especially interested, I think, in the chapter on "Rheumatic Nodules," but the whole book is a fund of information that is hard to obtain except by going through much of the literature. Incidentally, Findlay has consulted authorities on many of the subjects and has brought out all phases of any moot questions.

The book is well printed and brings a definite and valuable addition to the knowledge of the subject.

Maternity Handbook. The Maternity Center Association, New York City. Text prepared by Anne A. Stevens. Illustrated by Margaret Ayer. Price, $1. Pp. 178, with 112 drawings. New York: G. P. Putnam's Sons, 1932.

This book is based on the experience of the Maternity Center Association during the last fourteen years. It contains chapters on prenatal care and examination and advice to the expectant mother as to diet, clothes and choice of a physician. The concluding chapters deal with the babies' clothes and after-care and child training.

The book is full of valuable information to the mother, written in a simple, convincing way and profusely illustrated with clear drawings. It is an excellent book to advise the expectant mother to read.

Obstetric Education. Report of the Subcommittee on Obstetric Teaching and Education, White House Conference. Price, $3. Pp. 302, with tables and charts. New York: Century Company, 1932.

The report is divided into chapters on the obstetric education of physicians, nurses, midwives and the laity. For physicians it is recommended that more teaching instruction be given in obstetrics, and that fundamental requirements should be a measure of his ability as a specialist. The same applies to nurses and midwives. It is felt that the social worker has had insufficient training in medical social work. Prenatal and postpartum clinics under the charge of a physician should be established in all communities and should be closely linked with a well equipped hospital. The chapters are fully illustrated with charts and tables made from questionnaires received illustrating these points.

Fonctionnelles de l'enfant. By Henri Diffre. Price, 28 francs. Pp. 169, with 40 figures. Paris: Kaston Doin, 1932.

The author advocates physical exercises for many conditions in children. The book is based on physiology and is well illustrated with diagrams of the various exercises. The first part of the book deals with the obstacles to a natural life from our complex civilization; the second part, with physiologic conditions, and the third part, with practical applications.

Die Klinik des Diabetes mellitus im Kindesalter. By R. Freise and J. M. Jahr. Price, 4.80 marks. Pp. 57, with 4 illustrations and 3 tables. Berlin: S. Karger, 1932.

This publication comprises a separate section of volume 30 of A. Czerny's "Abhandlungen aus der Kinderheilkunde und ihren Grenzgebieten."

The authors review briefly the theory involved in disturbances of sugar metabolism, the clinical manifestations of diabetes mellitus in children and the method employed by them in the management of that disease. Their procedure differs from that usually employed in this country in the limitation of protein of the diet to a marked degree; 10 Gm. of protein daily is the amount prescribed in illustrative cases. The calorie allowance is about two thirds that recommended by Benedict and Talbot. A minimum of from 60 to 100 Gm. of carbohydrate is allowed daily. The authors stress the deleterious effects of mild infections in initiating latent diabetes or in aggravating the state of established cases.

This presentation will prove interesting to those already familiar with the treatment of diabetes in children, but it does not seem adequate as a guide to such treatment for the general practitioner.

Kinderheilkunde. By Dr. Franz Hamburger. Price, 12 marks. Pp. 268. Vienna: Franz Deuticke, 1932.

This textbook, as it quite frankly admits, is a short textbook for practicing physicians and students. The reading matter comprises 268 pages, and there are no illustrations. One can readily see that the material is greatly condensed, and that there is no superfluous matter in the volume. It is, however, an excellent volume, as one would expect from the eminence of its author, and has especially good chapters on the neuroses in childhood and an introduction to infections. A fair amount of time and space is devoted to the subject of infant feeding, and, taken all in all, it is an excellent presentation.

It starts out with a general portion the comments in which may be imagined. The second part consists of diseases of infants, taking up those of the new-born, nutrition, etc. The third portion takes up the avitaminoses; the fourth part, infectious diseases, the fifth part, diseases of certain organic systems, and the sixth part, neuroses.

The book fulfils well what it started out to accomplish.

Memento des divers modes de secours. Paris: Montevrain, 1932.

This little pamphlet is simply a résumé of the public work for children that is done in Paris. It details the different services. There is also a part given over to the service of old people, infirm people and patients with incurable conditions.

Enfants Assistés. Parts I and II. Paris: Montevrain, 1931.

This report consists of two parts: the first concerns the administrative side, and the second, the financial. In the first, a careful, complete report of all the work done in the various charities for children carried on by the city of Paris is recorded. This offers valuable statistics for reference.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Place: London. Time: July 20-22, 1933.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Henry Gauvain, 125 Harley St., W. 1, London.
Secretary: Dr. E. I. Lloyd, 33 Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Frederic W. Schlutz, Bobs Roberts Hospital, University of Chicago, Chicago.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Milwaukee. Time: 1933.

American Academy of Pediatrics

President: Dr. John L. Morse, 319 Longwood Ave., Boston.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.
Place: Detroit. Time: September 12-16, 1932.

American Pediatric Society

President: Dr. Oscar M. Schloss, 1185 Park Ave., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.

Canadian Society for the Study of Diseases of Children

President: Dr. G. A. Campbell, 164 Metcalfe St., Ottawa, Ontario.
Secretary-Treasurer: Dr. L. P. MacHaffie, 162 Clemow Ave., Ottawa, Ontario.

Society of Pediatric Research

President: Dr. Bengt Hamilton, University of Chicago, Chicago.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Kansas City, Mo. Time: October 7-8, 1932.

North Pacific Pediatric Society

President: Dr. A. Howard Spohn, 925 West Georgia St., Vancouver, B. C.
Secretary: Dr. L. Howard Smith, 734 Medical Arts Bldg., Portland, Ore.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Birmingham, Ala. Time: November 16-18, 1932.

STATE

Alabama Pediatric Society

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Charles E. Boynton, 118 Forrest Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

Louisiana State Pediatric Society

President: Dr. R. T. Lucas, Shreveport, La.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

Medical Society of State of New York

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester.
Secretary: Dr. Adolph G. G. De Sanctis, 12 E. 11th St., New York.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

North Carolina Pediatric Society

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. C. E. Bradley, Medical Arts Bldg., Tulsa.
Secretary: Dr. G. H. Harrison, 1200 N. Walker St., Oklahoma City.

South Carolina Pediatric Society

President: Dr. T. D. Dotterer, 1512 Marion, Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

Texas Pediatric Society

President: Dr. J. H. Park, Jr., 3717 Main St., Houston.
Secretary-Treasurer: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.
President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Joseph Golomb, 496 E. 17th St., New York.
Secretary: Dr. E. Leonard Benjamin, 2229 Valentine Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Henry E. Irish, 432 S. Lincoln St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Charles Wilson, 10 Peterboro St., Detroit.
Secretary: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: T. Bolling Gay, 384 Peachtree St., Atlanta.
Secretary: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. John Caffey, 50 Haven Ave., New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. Samuel Amberg, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelhia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, 724 Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. E. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Retreat for the Sick, 2621 Grove Ave. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 221 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. C. H. Platz, Fort Collins, Colo.
Secretary: Dr. R. H. Verploeg, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. Donald K. Woods, 2545 4th Ave., San Diego, Calif.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1932.